

Lame Ducks Come Home to Roost

MR JOHN DAVIES, the Secretary of State for Trade and Industry, is rapidly becoming the British government's fall guy. In the past year, he has been compelled publicly in the House of Commons to eat the words in which he proclaimed that his ministry was not in business to help lame ducks on several humiliating occasions, the most conspicuous of which was his announcement that the Upper Clyde Shipbuilders were to be given a government grant of £35 million (see *Nature*, 236, 49; 1972). Last week, he went the whole hog, on the second day of the debate on the budget for 1972-73, with an announcement of a new programme for channelling financial help to British industry which, especially in its proposals for regional development, closely resembles the earlier policies of the Labour government. Nobody should be surprised that Mr Davies's chief supporters in the House of Commons were members of the Opposition. It remains an open question whether the new policy will be successful.

The most immediately attractive of the new proposals is that companies investing in new plant and machinery should be allowed to set this off against their profits in a single financial year, with the result, of course, that in most cases the corporation tax will be handsomely reduced. Plainly, the government is worried that industrial investment has not sharply increased with the loosening of restrictions on the supply of capital in the past few months, and this, indeed, is a matter of common concern. Unhappily, this device of free depreciation is an attempt to cure the disease by treating some of the symptoms. If industries are reluctant to invest although money is comparatively easy to come by, what reason is there to think that the prospect of a saving on tax will make investments in new plant and machinery suddenly economic? To be sure, many companies will take this chance of replacing old equipment or of modernizing existing factories, which will bring an immediate improve-

ment to the prosperity of those who manufacture capital equipment of all kinds and, in due course, some improvement in industrial efficiency. By itself, however, it is unlikely that free depreciation will do much to encourage the creation of new industrial enterprises, the industries on which British prosperity should depend in the decades ahead.

Much the same doubts surround the other components of Mr Davies's package. First, it has been decided that in the economically backward parts of Britain, special areas and development areas as they are called, investment in new plant and machinery will be rewarded not merely with free depreciation but also with cash payments which may be as much as 20 per cent of the total sums involved. At the same time, there is to be set up an Industrial Development Executive within the Department of Trade and Industry to administer this system of incentives, to take over the department's regional offices and, through them, to provide help and advice for industries and local authorities and, with the help of an outside independent board, to determine some kind of strategy for the long-term development of industry. Mr Davies says that the executive will be asked, from its starting point on April 10, to investigate shipbuilding and the machine tool industry, two of Mr Davies's lame ducks. With any luck, the new organization could play an important and constructive part in the shaping of British industry. Its director, Mr L. I. Tindale, has a splendid reputation. The question which cannot be decided in advance, for it is intrinsically political, is whether the new organization will be more concerned with the future than the past.

It is only fair to say that the new arrangements, which resemble those of the Labour government in their proposals for regional development, are in other respects a vast improvement on the old Industrial Reconstruction Corporation. It was also a paradox that a Labour government should have based so much of its industrial strategy on the principle that large companies are intrinsically more desirable than small companies. To be sure, Lord Blackett's argument that too much of British industry has in the past skimped on research and development, so that amalgamations between companies might be expected to produce organizations with research departments large enough to be effective, remains valid but this is only a part of the story. Experience has shown that many of the marriages arranged by the IRC, sometimes at gunpoint, have been less successful than their originators hoped, often because they have created conglomerates of diverse activities when smaller and more specialized industries would have been more able to keep afloat. But at least the IRC was empowered to discriminate between companies in particular fields and was able to concentrate its attention on fields which seemed to matter.

The danger in the new arrangements is that the Industrial Development Executive will have to abide by

Conference on the Environment

Nature and the Royal Institution will hold a conference on environmental problems at the Royal Institution, Albemarle Street, London W1, from 1.45 to 5.45 p.m. on Friday, April 28, 1972.

Speakers will include Dr K. C. Dunham (Institute of Geological Sciences), Dr Kenneth Mellanby (Monks Wood Experimental Station) and Dr William Brass (London School of Hygiene and Tropical Medicine).

Applications for tickets (up to 2 per person) should be sent to: *Nature*/RI Conference, Macmillan Journals Ltd, Little Essex Street, London WC2R 3LF. Tickets will be free but applicants are asked to send a stamped self-addressed envelope.



the rules laid down for regional development, with the result that many unsuccessful companies will be kept in business when they should be in Carey Street. When it comes to fostering the development of industries which are in trouble (such as machine tools) or industries which have great potential for the future, the executive will no doubt be forced back on systems for direct subvention which are indiscriminate or on the device of government purchasing (now to be used in the machine tool industry). And this, of course, is the point at which political pressures will be most acutely felt. If Mr Davies has abandoned his stern view of lame ducks, there is no reason to suppose that other interests, the members of the House of Commons included, will follow suit.

Which are the fields in which new opportunities might be found for British industry? Over the years, it has become apparent that industrial innovation has been hampered not so much by lack of inventiveness or even lack of capital as by a failure to sell new products efficiently in countries overseas or even in Britain. In the 1940s, for example, Britain ran a good second to the United States in the development of electronic computers but now, in spite of the attention lavished on the computer industry by the IRC, International Computers Limited is still protesting that it will need further government subventions to become competitive. In the early 1950s, the British nuclear power industry was proud of its achievements and over-confident of its future, but now there is again a serious risk that it will fail to sell its products successfully. In electronics, British companies have been diligent but unspectacular and not especially profitable. In telecommunications, they have been unfairly handicapped by the monolithic purchasing power of the Post Office as well as by their own insularity. The metallurgical industries have grappled bravely with innovations but have often failed to identify a market for them. Why have so many bright ideas run—in commercial terms at least—into the sand? One of the simplest explanations is that too many new developments have been started in innocence of the potential market. Another problem has been the difficulty of persuading British engineers that commercial salesmanship of technical products is not a tedious and demeaning chore but an essential part of any commercially founded enterprise.

There is no obvious way in which the new arrangements worked out by the Department of Trade and Industry will help in this direction. The government may say, with some justification, that these are matters for companies themselves to organize. Yet in several important fields the government and public corporations have an important influence. The complicated relationship between the Central Electricity Generating Board

and the Atomic Energy Authority, to mention only one example, provides an awkward umbrella for manufacturers of nuclear equipment, but in any case the authority could be, if it chose, a more vigorous salesman on behalf of fast reactors, with the successful development of a prototype now in prospect. There are also important tasks which can be tackled within the fields of operation of the Post Office and the British Steel Corporation, and nobody should be surprised if one of the first frustrations of the Industrial Development Executive is that of not having direct access to these nationalized corporations. But where the general run of industry is concerned, the most immediate need is that small enterprises should be given help in selling what they make or wish to make, not so much through the genteel agency of the departments of the old Board of Trade now absorbed within the Department of Trade and Industry, but directly, by the provision of help with the strengthening of the commercial activities of small enterprises in fields such as scientific instruments. If subventions for the purchase of plant and equipment are now in order, may it not also be appropriate that the government should help with this kind of development as well?

The most obvious omission from what Mr Davies had to say last week is research and development. Since the publication of Mr Anthony Wedgwood Benn's green paper in 1968, which floated as successfully as a lead balloon even within the sympathetic framework of the Labour government's policy, virtually nothing has been heard of this important topic. The reorganization of the Atomic Energy Authority is still incomplete. It seems to be assumed that industries, public and private, will hire whatever resources they may need. But in reality, there is now far too little creative work being undertaken to ensure that British industry will be competitive in fields yet to be developed. But if plant and machinery in development areas are now to qualify for an extra 20 per cent grant, is there not at least a case for thinking that research and development might be a similar case? Is it not high time that the government evolved a coherent strategy for industrial research and development outside the public sector? What, for example, is the future of the research associations? What is to be done to canalize the work of the research establishments at Farnborough and Malvern to productive enterprise? And which part of the government machine is to seek to influence the way in which the pattern of research and development evolves? It is one thing for Mr Davies to welcome his lame ducks back from the spartan hill-sides to which they had been consigned, but why does he so studiously ignore that part of industrial activity on which the future of British industry must rest?

Magruder's Mouse Emergent

PRESIDENT NIXON's Technology Message to Congress two weeks ago (see *Nature*, 236, 137; 1972) will disappoint Mr William Magruder's friends and admirers but should be a warning to those who may be tempted to think that science and technology can by themselves and without much difficulty bring industrial innovation and company profits. Although there is a need that Mr John Davies in Britain (see above) should pay some attention to this

intractable problem, he will at least know now that there is no purpose in following the brash course on which it seemed, six months ago, that Mr Magruder had been set by the President of the United States. The idea then was to develop a series of programmes designed to stimulate industrial innovation and, at the same time, to help with the solution of pressing problems, social and economic. In the event, the Administration seems wisely

to have decided that these are exceedingly difficult questions which cannot be answered without study and experiment. Moreover, the President appears to have settled for a form of organization that will not disturb the present relations between the Office of Science and Technology at the White House and the National Science Foundation and the Department of Commerce, both of which have a finger in the pie of industrial innovation and development. So far, so good.

The biggest stumbling block in the years ahead is likely to be the difficulty of finding an alternative for the system for supporting industrial research and development in the United States which has been such a conspicuous success in recent decades. For the most part, the United States government has been able to forward the cause of industrial research and development in the United States by using its massive research and development programme in defence and space technology to provide a steady stream of development contracts. The result has been that companies large and small have been given not merely the funds needed to equip laboratories but also an incentive to develop particular products. With the inevitable decline of expenditure on defence and space, and with nuclear energy also running down, this source of funds is steadily diminishing. The question which the Administration has somehow to answer for itself is whether it will be feasible, in the years ahead, to create arrangements for stimulating research and development without this steady stream of project-oriented contracts. In short, the United States will have to develop systems for stimulating innovation which are very much like those much needed elsewhere in the world.

What, then, of the proposals put forward last week in the message on technology? The notion that the Department of Commerce should become the cornerstone of the Administration's intervention in private industry is sensible enough. Partly at least because of its control of the National Bureau of Standards, the department is well placed to play such a part. But political strength as well as cleverness will be needed if the department is somehow to avoid the difficulties which have bedevilled similar attempts elsewhere. What will happen, for example, if the aircraft industry, now unexpectedly falling on hard times, sets up a clamour for government assistance in research and development in much the spirit in which the American shipbuilding industry has been able to win subventions for itself? How rigorous will the Department of Commerce be in saying that its real concern is with innovation and not with the support of industries whose markets have, for one reason or another, become attenuated? By all accounts, the department has in mind a variety of schemes for setting up collaborative research projects, but here again there are lessons to be learned from experience elsewhere, especially in Britain. After all, nobody has been able to devise a way in which companies will pool their efforts in research without at the same time fearing that they will have put their commercial future in jeopardy. One of the consequences has been, in British experience, that larger members of research consortia always supplement the common programme with larger research programmes of their own. No doubt a large part of the trouble is that the research associations in Britain have been too securely institutionalized. The Department of Commerce might be better advised to encourage *ad hoc* arrangements for collaborative research.

The National Science Foundation's role in the new technology assistance framework is harder to define. Its chief efforts so far have been in encouraging closer collaboration between industry and the universities, sometimes with the help of matching grants. But the foundation also has its nose buried deeply on the trail of projects that will have some national importance. Its shopping list includes projects such as transport, the cleansing of the environment and the amelioration of earthquake damage. The trouble is that there is no easy relationship between these entirely desirable objectives and the future prosperity of the United States, which goes to show that it will be hard for anybody, Mr Magruder or the Department of Commerce, to base a continuing programme for the support of industrial innovation on the experience likely to be gathered by the National Science Foundation in the next few years. In short, the Administration has been wise to be cautious but, even so, it may not yet have realized the full magnitude of the task that it is attempting.

100 Years Ago



The Adamites

PHILOLOGISTS will notice with regret a paper bearing the above title in the late number of the *Journal of the Anthropological Institute*. The author appears to have taken up, without proper study, that difficult and dangerous line of argument, the comparison of historical names, and has naturally fallen into the network of delusive fancy which in past generations entangled Jacob Bryant and Godfrey Higgins. Modern philology has abundantly proved that slight, loose, and occasional correspondences in proper names are deceptive as evidence, even among languages of the same family, much more among languages of different families. It is a fair sample of the present paper, that it argues an affinity between the peoples of the Old and New Worlds on the basis of a connection between various names of the Deity, among which are the Russian *Bog*, the Mantchoo *Ab-ka*, and the Hottentot *Tigwa*. The special purpose is to prove that nations are shown by their names to trace descent from an ancestor called *Ad*—“Adam, or Father *Ad*.” Thus “the great Hamitic race of *Akkad*” is interpreted by the aid of Welsh *ach*—root, lineage,” so as to mean “sons or lineage of *Ad*”; and the name of *Ta-ata*, the Polynesian First Man, is “that of the mythical ancestor of the Adamites, reversed, however, and with the addition of *ata* (*aka*), spirit”! It is obvious, though unaccountably overlooked in the paper, that two of the clearest cases of the theory may be found near home. The descent of two nations from Father *Ad* is perfectly recorded by ourselves, when we call the representative of one a *Paddy*, clearly *Ap-Ad* (from *Ap*, “used in the sense of son”), while the other's Adamite ancestor is commemorated by calling his descendant a *Taffy*.

It is not necessary to give the name of the author of this unlucky paper. Everybody is liable to slips, great or small; and a man may have done work worth doing in one line, but turning suddenly to another, may come to grief utterly. But the Council of the Anthropological Institute should have consulted their own interest and that of their contributor by declining to print the present essay. It is the duty of a learned society to examine even a hasty and ill-considered idea brought forward by one of its members, but not to put it on public record against themselves and him.

M. A. I.

OLD WORLD

Select Committee Reaches the End of the Road

AT the penultimate hearing of the Select Committee on Science and Technology last week, the committee's doubts over the science policy of Britain were exposed. The select committee has for the past nine weeks been attempting to discover what that policy is, but has been unable to find an answer that satisfies it. On the Wednesday morning the select committee had before it Sir Alan Cottrell, the government's chief science adviser, Lord Jellicoe, Lord Privy Seal, and for the second time Sir William Pile, permanent secretary at the Department of Education and Science—although in the event Sir William hardly got a word in.

Sir Alan explained that there is a policy for basic science that covers the research councils, but the responsibility for departmental research lies with the various departments. The amount that they spend on research is decided vertically by examining, for example, how much is spent on transport and then spending on transport research accordingly—not by comparing transport research with, for example, fisheries research, and deciding how much to spend on each—which would be a horizontal policy. The select committee then asked if the government had goals towards which scientific research was directed. Sir Alan said it had, but was unable then to define the resultant policy except by saying it is the combination of the work done by all the departments. Mr Airey Neave retorted that "that is no answer", and said that Sir Alan was in fact implying that there is no research and development policy for Britain. Sir Alan naturally enough denied this, saying that in his opinion research in the departments is answering the nation's needs. If all the research within the departments were taken from them and put into one horizontal policy, which crossed departmental boundaries, then, said Sir Alan, "you would make a hash of the research".

The select committee was, however, plainly dissatisfied. It took the example of space research and said that it thought there should be a national policy for space, rather than mini-policies by each department to suit their individual needs. Sir Alan replied that the policies should be coordinated, but "to pull the space work out of the various departments and put it all into a space agency would not serve the best interests of the

nation". Lord Jellicoe said that he agreed with the philosophy of this approach; governments do have goals which they approach through the departments, while on basic science they do have a horizontal approach.

But the committee still wanted to know who makes the long term judgments on scientific research and who decides where the priorities lie. Sir Alan replied that there is a policy for science within each department. The select committee then asked how, if there was a clash over funding for research on aerospace and on nuclear power, was that clash resolved? Sir Alan replied that it would be a decision at cabinet level, but would rest on establishing a power programme and an aerospace programme, and then settling how much of each programme goes on research.

When the committee turned its attention to the Rothschild report, Lord Jellicoe said that the government had only committed itself to the customer-contractor principle and its application to applied research and development in the research councils and government laboratories. It was also committed to a strong and viable research councils system and the continued existence of the Council for Scientific Policy or some modification of it. The committee also questioned Lord Jellicoe at some length on the wisdom of commissioning just one man—Lord Rothschild—to undertake such a far reaching inquiry. Lord Jellicoe replied that the green paper consisted of two complementary reports which meant that the problem could be examined as if

through bifocals. He said that he personally found Rothschild's prose style "rather refreshing" and pointed out that Rothschild, as a scientist, ex-chairman of the Agricultural Research Council and with experience of government, was eminently well qualified to produce the report. He admitted that the report could have been produced by the Central Policy Review Staff rather than just by Lord Rothschild, but pointed out that Lord Rothschild could have involved the CPRS if he had so wished. Lord Jellicoe vigorously denied the suggestion put to him by Dr John Cunningham that Lord Rothschild was chosen to produce the report because his views were well known to the government which wanted those views propounded. Lord Rothschild was not chosen, said Lord Jellicoe, "with malice aforethought".

Lord Jellicoe also pointed out that there had been a great deal of controversy over the report, which he felt to be no bad thing. There had been no shortage of consultation by the government with the parties concerned, and the discussion provoked was a healthy one. Sir Alan Cottrell had received over 400 submissions on the report, and although the official period of consultation is over, Lord Jellicoe said that he would still be happy to receive people's comments.

In the afternoon the select committee turned its attention to Lord Zuckerman. The atmosphere was calmer and more measured as Lord Zuckerman said that he felt there was a need for established definitions of basic and applied science—he had in fact already offered one as long ago as 1961 in the Gibbs-Zuckerman report.

Lord Zuckerman did not think that the Council for Scientific Policy would be the right body to do the long term thinking for government research and development because it has no control over scientists within government departments. Lord Zuckerman doubted if a body with executive responsibility could be set up over the departments' heads to deal with research and development, but Lord Zuckerman implied that he was very much in favour of a central advisory body. He did not, however, favour Dainton's proposed Board of the Research Councils; it would not, said Lord Zuckerman, have the full impact which Sir Frederick Dainton envisages.

THE Select Committee on Science and Technology which has been taking evidence from witnesses for the past nine weeks on the reports of Sir Frederick Dainton and Lord Rothschild which were published in the green paper, *A Framework for Research and Development*, intends to report to the House of Commons on March 30, according to Mr Airey Neave, Chairman of the Select Committee.

Lord Jellicoe, Lord Privy Seal, said last week that the government hoped to produce its white paper on government research and development in June.

OCEANOLOGY

Technological Jamboree

A VISIT to the Oceanology International 72 Exhibition in Brighton left a bewildering impression of an array of technological advances and techniques which made it difficult to keep in mind how these pieces fit together and relate to the worldwide problems of how to make the best use of our environment. Of course, there was a parallel conference with the theme of "Ocean Management", and that provided a better opportunity to understand the impetus behind Oceanology 72 and the reason why so many technological trees are flourishing in this particular wood.

But just as it is difficult to believe that international motor shows are instrumental in selling cars, so it is difficult to believe that exhibitors came away from Brighton with order books stuffed full of requests for echo sounders or desalination plant.

There were, however, several items exhibited which are of particular interest to anyone who has worked in the ivory towers of university research. Perhaps the shining example of a piece of research which is beginning to find a niche in the technological world is that of the laser. No longer is this a solution searching for a problem, and indeed many of the problems which can be solved by laser applications are related to the oceans. Survey lasers which can replace theodolites have already been used successfully for tunnelling.

There is an obvious need for similar systems for marine use—in particular, any technique which can improve the efficiency of dredging operations, by providing an accurate line to steer by, would be a welcome addition to the repertoire of inshore operators. In this case, the immediate problem to be solved has been that the laser is, in a sense, too accurate. Once a dredging vessel strays out of the beam it requires some skill on the part of the crew to find it again. Now, Decca has found what appears to be the solution, and in its new marine channel lights it makes use of two HeNe lasers with spread overlapping beams. One of these lasers is on for 0.5 s and off for 1.5 s, while the other flashes intermittently for 1.5 s at a time with pauses 0.5 s long. In this way, a continuous beam is seen only in the required line of sight; as the vessel begins to stray this changes to a flashing light, and the spacing of the flashes immediately indicates the direction of the error. Such a system also has immediate application to navigation (of aircraft as well as ships).

If the laser is an example of pure research becoming applicable to technology, there are also examples of technological developments which aid research almost accidentally. One

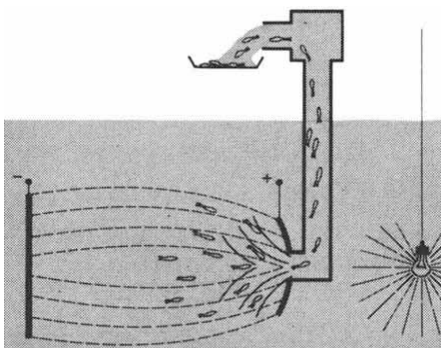


Fig. 1 Electrical ocean fishing system being developed by ACB de Bretagne. Fish are lured towards the suction nozzle of a pump by a bright light and a pulsating electrical current.

example of this which was on view in Brighton is a bottom sounder, developed by Raytheon Ocean Systems Center, which is so sensitive that it detects individual fish in the sea above the ocean bottom. To the oceanographic surveyor this is an irritation to be regarded as noise, as is the scattering layer (the nature of which is not yet clear) often recorded on these sounding charts a little way below the ocean surface. But one man's noise could be music to other ears, and the ingenious minds behind the fish trap shown in Fig. 1 might well be among those interested in an improved technique for recording the movements of fish.

ENGINEERING MATHEMATICS

Growth Encouraged

SOME British engineering graduates are falling behind their European and North American colleagues in mathematical ability, according to a report from the Science Research Council's Engineering Mathematics Panel (Science Research Council, 1972). The panel says that this situation could be improved if mathematical engineering were encouraged as a discipline, and if there were more interchange both between the universities and industry and between mathematics departments and applied science departments within universities themselves.

Since the Engineering Mathematics Panel was set up in 1969 under the chairmanship of Professor A. Jeffrey of the University of Newcastle, it has been discussing the problem of how to encourage research and training in engineering mathematics with each of the SRC's seven engineering committees and panels. The panel particularly recommends the organization of more joint university/industry study groups along the lines of those run in Oxford by Dr A. B. Tayler. Dr Tayler's groups each consist of up to twenty people, about half from the Oxford mathematics department and half from industry;

ECONOMY

More Machine Tools

MR JOHN DAVIES, Secretary of State for Trade and Industry, announced in the House of Commons last week that in order to assist the machine tool industry the DTI was granting £4-£5 million to polytechnics and colleges of education. The Department of Education and Science would also inject £1 million into universities — through the University Grants Committee—for the same purpose.

Mr Davies's statement in the Commons did not make clear to what precise use the money was to be put. A spokesman for the Department of Education and Science expressed complete ignorance of the existence of the grant and so he was unable to say whether it was to be used for research or for the purchase of capital equipment. Similarly the Department of Trade and Industry was unable to throw any light on the question.

The fate of the £1 million allocated by the DES finally came to light when a spokesman for the UGC—after much searching—announced that it was to be used for the purchase of machine tools within universities. Presumably the £4-£5 million that will go to the polytechnics and colleges of education will be used for the same purpose.

during a study meeting (usually lasting a week or two) the industrial participants raise some of the mathematical problems which have arisen in their own companies and these are then investigated by the whole group. The report says that these group meetings have thrown up problems ranging from those which make useful undergraduate exercises to those suitable as PhD topics or, sometimes, as longer term research projects.

The panel is also impressed with the way in which the engineering mathematics studentship scheme is developing. Under this scheme mathematics departments can apply for special studentships which enable graduate mathematicians to move into applied science departments. The panel thinks that the scheme should be expanded and given further publicity. Mathematics and engineering departments are encouraged by the panel to make joint applications for SRC research grants when appropriate, and engineering departments, the panel says, should carefully consider the inclusion of mathematicians in research teams—especially those teams involved in the study of transportation systems, for example.

Intensive short courses in universities to acquaint industrial mathematicians and engineers with new mathematical techniques are also recommended.

ENVIRONMENT

A Burning Issue

It is clear that the British government is soon to take the first steps towards its long promised regulation of car exhaust emissions. As long ago as December 1970, Mr Peter Walker was making vague promises about limiting exhaust emissions, and it seems that the first step will be the reduction of the permitted lead levels in petrol by 25 per cent.

This reduction, however, is simply paying lip service to the real problems. The average lead level in British petrol in 1971 was 0.54 g l.⁻¹. The current permitted lead level is 0.84 g l.⁻¹, and following the 25 per cent reduction—if that is all it proves to be—that level will drop to 0.635 g l.⁻¹; such a reduction will make little or no difference to lead levels in Britain. Even the lead levels of five star petrol—which forms a comparatively small part of the total sale—were only 0.64 g l.⁻¹ last year.

Last year British cars swallowed 14.5 million gallons of petrol and in so doing put 9,000 tons of lead into Britain's air. Yet there is no evidence to show that the lead levels found even in the busiest streets in Britain are dangerous to adults.

Nonetheless the cry for the removal of lead goes up, and when it comes to environmental issues in politics it is one of the easiest bandwagons upon which to jump. But if lead is to be removed, people must be prepared to pay. Removing the lead from petrol completely would involve building £200 to £250 million of extra refining plant in Britain alone. There would be smaller amounts of high octane petrol available, and virtually no five star grade. A gallon of petrol could cost between 2p and 3p more, which would put between £5 and £10 on the average motorists' annual petrol bill and between £80 and £120 million on Britain's. Alternatively, the compression ratios of cars could be lowered and lead free petrol used. The result would be a 10 per cent fall in efficiency or a ten per cent increase in the amount of fuel used if efficiency is to be maintained.

Lead is put into petrol—and has been since 1925—as an anti-knock agent. It is the simplest and cheapest method known to raise the octane level that modern high compression cars demand.

The call for its removal is on two counts. First, that lead is cumulative both in the environment and man; and therefore pouring 9,000 tons of it into the atmosphere a year cannot be a good idea. Second, lead damages the catalysts that various companies are trying to develop to remove the hydrocarbons, nitric oxides and carbon monoxide from exhaust gas in order to meet the 1976

Federal emissions standards in the United States. These are 0.41 grams of hydrocarbon per mile, 3.4 grams of CO per mile, and 0.4 grams of oxides of nitrogen per mile. These figures represent a fall of 90 to 95 per cent on uncontrolled emissions.

At present European standards are generally easier than the proposed American ones, but there is no doubt that Europe will follow America's lead.

In the short term the best hope of meeting the 1976 standards seems to lie in "hang-on" devices. These involve exhaust gas recirculation, injecting air into the manifold or attaching catalysts to the exhaust system to render the gases harmless. Because of the possible financial returns on a successful catalyst many companies are examining the last possibility. The biggest fly in the ointment as far as these are concerned is that one of the rider clauses to the 1976 levels is that the catalyst system must last 50,000 miles. Apart from the problem that to test a catalyst under real road conditions takes the best part of a year, there is also the problem that many exhaust systems fall apart before the car has travelled 50,000 miles.

The chief problem with exhaust gases is the oxides of nitrogen. The carbon monoxide and hydrocarbons can be dealt with efficiently by oxidation, but removing the nitrides of oxygen is more difficult, although it can be done, but probably not for 50,000 miles and probably not cheaply. British Leyland and ICI have developed a system that looks promising, and Shell among others is also working on the problem. No one has yet tested any system successfully to 50,000 miles, and current estimates put the extra cost per car for any foreseeable catalyst in the order of £100.

In the long run—and maybe even in time to meet the 1976 standards—there may well be other, more radical answers to exhaust emissions, involving major redesign of the internal combustion engine, electric or diesel engines, or the limited use for car fleets of liquefied natural or petroleum gas.

One of the most promising ideas is a lean mixture system being developed by Shell at its Thornton research centre. The compression ratio of most cars is about 12:1, but by producing a perfect mixture of air and fuel and feeding it to the engine Shell has succeeded in getting a car to run perfectly in the laboratory at a ratio of 22.5:1. (A normal car would be backfiring severely at about 17:1.) With this system the emissions fall dramatically, although hydrocarbon emissions remain high, but Shell points out that this is less of a problem than having to remove excess oxides of nitrogen. There is, however, a serious power loss with the system (this could be overcome by increasing engine size) but there is also a consider-

able saving of petrol, because the mixture is so lean. At the moment the system consists of 2 tons of laboratory equipment which needs shrinking to an acceptable size and fitting with a revolutionary carburettor which someone has yet to design. It is clear that, however it is done, clean air is going to cost.

UNIVERSITIES

Five Years On

THE time is drawing nearer when Mrs Margaret Thatcher, Secretary of State for Education and Science, must decide on the future of the universities for the next quinquennium, but there are, as yet, few indications of what is in her mind.

The announcement of the allocation of resources—which are distributed by the University Grants Committee—must come by the autumn of this year, although it is possible that the announcement could come towards the end of the next session of Parliament. The UGC has put its submissions to Mrs Thatcher, and the universities must await the outcome.

The student numbers towards which the universities have been working are 320,000 by 1976/77, compared with the 234,000 in universities this year. This is the figure suggested by the UGC in its preliminary memorandum of guidance, but the government is in no way tied to this figure. Memoranda from the Committee of Vice-Chancellors and the Association of University Teachers among others have made it plain that to many this figure is the minimum acceptable. There have, however, been rumours—and they are only rumours—that this figure may be cut to 305,000 by 1976/77. The universities have to compete for funds not only with the polytechnics, but also with the colleges of education and the schools, within the education budget. Added to this there is the current difficulty in finding jobs for graduates to the extent that 9 per cent of last year's applied science graduates and 6 per cent of pure science graduates were still unemployed in December.

Whatever the final numbers, it seems likely that the largest expansion will be in the arts, not the sciences. The buildings already in existence for science and technology will be able to handle the expected increase in science students, and it is in science that the unused capacity in the universities lies. For science, the next quinquennium looks like one of consolidation, not expansion. Further, the spare capacity is likely to be used for undergraduates rather than postgraduate work. It is certainly the opinion in some university science departments that the money for research is going to have to come increasingly from the research councils and industry.

NEW WORLD

Pipelines, Pollution and Prosperity in the Tundra

by our Washington Correspondent

If the extent of oil deposits along Alaska's North Slope had been realized just a few years earlier, hot oil would probably now be flowing through a pipeline across the Alaskan Tundra. Unfortunately for the oil companies involved, who have 800 miles of pipe rusting in base camps across Alaska, but fortunately for the Alaskan wilderness, the oil strike coincided with the present concern over the environment in the United States, and a proposal to pipe hot oil from wells in Prudhoe Bay in the Alaskan Arctic to the ice-free port of Valdez has precipitated a two-year war of attrition between the oil companies and various environmental groups.

The end of the dispute may now be near, for last week the Department of the Interior dropped in the laps of the contestants its long-awaited final statement on the environmental and economic impacts of the pipeline. Those concerned have thirty days in which to digest the report's 4,600 pages and to offer comments to the Council on Environmental Quality. It will then be up to Rogers C. B. Morton, Secretary of the Interior, to decide whether or not federal lands will be leased to the oil companies. Morton said last week that he needs "at least 45 days" to come to a decision.

The proposal, which was set out in detail last year by Alyeska, the consortium of oil companies hoping to build the pipeline, entails construction of a 48-inch diameter pipe from the North Slope oilfields to Valdez—a distance of 789 miles. The pipe would eventually carry up to 2 million barrels of crude oil a day, at a temperature of about 80° C, and for some 55 per cent of its journey it would be buried eight feet beneath the surface.

It is difficult to imagine a proposal more calculated to inflame the passions of environmentalists. Not only would the pipeline cut a swathe across the Alaskan wilderness—America's last frontier is the phrase—but it would entail the building of a road deep into the tundra region, thereby opening up the area for hunters, and it is also likely to pollute the North Pacific Ocean with intentional and accidental tanker discharges. But the oil companies, one of the most powerful lobbies in Washington, have been able to point to the economic benefits of exploiting the

North Slope oil, and Alaskans have also been four-square behind the proposal for the oil revenues it will bring in. The whole debate finally came to a head early last year when the Department of the Interior (which has the responsibility for leasing the lands for the pipeline) issued its draft environmental impact statement on the project.

The draft statement concluded that "construction and operation of the proposed trans-Alaskan pipeline in accordance with the Department of Interior stipulations and all applicable laws and regulations relating to environmental protection would reduce foreseeable environmental costs to acceptable levels". The department got its knuckles firmly rapped by environmentalists, who charged, during a bruising inquiry into the proposal, that the department had skimmed on its studies and was merely using the statement to support a decision already made. That may be why the final statement is much more equivocal, offering no recommendations and presenting a detailed, matter-of-fact analysis of the likely environmental consequences of the project. And nobody can accuse the department of not being thorough—nine volumes of analysis testify to that*.

The chief conclusion reached in the statement is that "no single oil delivery system would be free of environmental effects and of potential threats", but according to William Pecora, the Undersecretary of the Interior who supervised the study, "the question is whether the impact can be minimized to an acceptable level". In short, what the statement suggests is that the proposed pipeline will produce inevitable geological disturbances resulting largely from damage to the permafrost region both by destruction of the vegetative mat and by heat from the pipe, that

terrestrial mammals such as caribou will suffer because the pipeline will present an obstacle to their seasonal migrations and grizzly bears would probably suffer from sharing their environment with construction workers and hunters. There are hazards for freshwater fish from possible oil spills, especially if oil finds its way under the ice.

Perhaps the chief danger to wildlife stems from the proposed tanker traffic from Valdez to ports on the West Coast. Chronic pollution from oil discharged during tanker cleaning operations and in accidental spills would "have permanent and far-reaching effects on certain forms of plankton", the statement suggests, and it could also pose a serious threat to the pink and chum salmon which spawn around Valdez. The dangers from tanker collisions are obvious, and could have a serious effect on the Canadian coastline. The Department of the Interior has calculated that on average accidental spills will put about 140,000 barrels of oil a year into the environment.

As for accidental spills from the pipeline itself, the statement points to two possibilities. First, two-thirds of the pipeline will run through a seismically active region, in which it is "almost a certainty" that one or more earthquakes of magnitude 7.0 will occur during the lifetime of the pipe and that a break could occur from a large ground displacement. The second and more predictable, if less tractable, problem lies in the engineering difficulties associated with construction in the permafrost region. The problem is that if the surface vegetation over a layer of permafrost is disturbed by construction of the pipeline, some insulation will be lost and differential thawing may occur in the summer months. This may cause ground slippage, especially in regions where the underlying soil is rich in ice. An associated problem is that since oil will enter the pipe at about 80° C, and will remain at about that temperature because of frictional heating as it is pumped along the pipe, the ground beneath it will thaw gradually.

The many difficulties involved in constructing a pipeline across hundreds of miles of Arctic tundra have, in fact,

*Available from the National Technical Information Service, Department of Commerce, Springfield, Virginia 22151. Six volume environment statement \$30, three additional volumes of economic and strategic analysis \$12.50.



already forced Alyeska to make several basic changes in its original plans. It was once hoped, for example, that the pipeline could be buried for some 90 per cent of its journey through Alaska, but the risk that the hot pipe would cause ground slippage and catastrophic changes in soil structure in ice-rich areas of permafrost has compelled Alyeska engineers to plan for a substantial amount of the route to be above ground—present suggestions are that nearly half the pipeline will rest on the surface on thick gravel beds or on piles frozen into the ground. This has in turn increased the barrier effect to large migratory animals, it will make the pipeline more of an eyesore, and it will involve substantial quarrying operations along the flood plains of rivers and increased damage to the vegetative mat by transporting gravel to the pipeline.

The first reaction of many of those who oppose construction of the pipeline was not to look to the report for an answer to that question, but to turn to the analysis of the likely environmental and economic consequences of running a pipeline from the North Slope into Canada, down the Mackenzie River Valley and eventually to Chicago and the midwestern United States.

The so-called Canadian Route has, in fact, recently become the battleground for opposing environmental and economic philosophies on exploitation of North Slope oil deposits, and there is mounting pressure on Mr Morton to wait until a thorough study of possible Canadian routes has been completed before he makes a firm decision on Alyeska's proposal for the Prudhoe to Valdez route. The environmentalists have argued that the Canadian Route should be studied because it would avoid the seismically active region of Alaska, it would not involve tanker transportation and would thus rule out any possibility of oil spill damage to the North Pacific and it would bring Alaskan oil to the midwestern and eastern states where oil prices are generally higher than on the west coast.

The most compelling argument for taking a close look at Canadian routes rests on the assumption that oil companies will almost certainly choose to pipe natural gas from the North Slope through Canada rather than across Alaska. If a gas pipeline is to be constructed, then would it not be sensible to build an oil pipeline along the same route at the same time? The Department of the Interior's Impact Statement carefully chooses not to answer that question, but suggests that the Canadian Route would be preferable if protection of the marine environment and avoidance of earthquakes are desired, while the Alaskan route would cause less terrestrial disruption.

Another factor that the report brings out is that the development of potential oil resources in the Canadian Arctic may eventually call for development of a Canadian oil pipeline.

Because there is as yet no formal proposal to build a pipeline across Canada to the midwestern states, the environmental impact statement is necessarily less detailed in its discussions of the likely environmental consequences of that construction. Nevertheless, there is sufficient material in the report for environmentalists to argue with some conviction that a decision on the Alaska pipeline should be delayed at least until extensive studies of possible trans-Canadian routes, now being carried out by the Canadians are complete.

Of the possible routes that a pipeline may take across Canada, the impact statement suggests that the one which goes inland from Prudhoe Bay to Fort McPherson, then down the Mackenzie River Valley to Edmonton, would be environmentally the most favourable for construction. The first leg of this route traverses Arctic tundra regions of Alaska and Canada's Northwest Territories, and would pose considerable engineering problems associated with the permafrost. In addition, gravel pits and haul roads to the pipeline would scar the vegetation, raising environmental hazards similar to those that would be encountered by construction of the trans-Alaska pipeline. This part of the route also crosses the Arctic National Wildlife Range.

As for the section of the possible pipeline route from Fort McPherson to Edmonton, ice rich permafrost in the northern portion would be a hazard and land slumps and slides could occur in parts of Alberta where there are steep slopes and clay shales. Such land movement, the report notes, would leave long lasting scars on the landscape. Other hazards are forest fires, and siltation of the rivers that would be crossed. But the report also points out that there are no known concentrations of fish resources north of Alberta which might experience heavy adverse impact from the pipeline development, and pipeline construction south of Alberta would be more routine and therefore less risky and, moreover, socio-economic impact would be relatively light since most of the area north of Alberta is sparsely occupied and little developed. And, as a parting shot that cannot fail to be missed by proponents of the Canadian route, the statement suggests pipeline transport systems probably will be built before long in this corridor. No ifs or buts.

Environmental considerations alone will not, however, decide the route of the pipeline. Other factors will be considered; clearly the most critical questions to be answered concern the costs of delaying a decision while alternative

routes are studied, how much longer it would take to bring oil to market through the Canadian route, compared with the trans-Alaska route, and finally, how each route will affect the price of oil in various parts of the United States.

The chief findings of the analysis are that by 1980 the difference between demand for oil in the United States and domestic production is likely to be running at about the level of 12 million barrels a day, and while four million barrels may be supplied from other countries in the western hemisphere, the remainder of the shortfall must come from the eastern hemisphere. The conclusion therefore is that North Slope oil will simply displace foreign imports, thereby helping balance of payments and national security. As for estimates of the cost of delays the statement provides a very gross estimate of between \$100 million and \$1,260 million and the only estimate of the time it would take to bring oil to market by the Canadian Route is attributed to a letter to the Department of the Interior from General George A. Lincoln, director of the Office of Emergency Preparedness. Lincoln estimates that the Alaska pipeline could bring oil to the market three years earlier than any alternative. No basis for the conclusion is, however, contained in the statement, although this question is now under consideration in the Department of the Interior. Finally, the economic analysis concludes that pipelines through Alaska and through the Mackenzie Valley would be equally efficient as far as transportation costs are concerned.

The publication of the voluminous impact statement now leaves the ball very firmly in the court of the Secretary of the Interior. Morton has essentially three alternatives. He can agree to the application for federal lands for the construction of a trans-Alaska pipeline, or he can deny the application. His other course of action would be to delay a decision until other alternatives have been thoroughly analysed. Whatever decision he takes, however, will certainly be hotly challenged and he is already faced with a court injunction barring issuance of permits for construction of a road alongside the pipeline. Moreover, there will now be a clamour for more public hearings on the final impact statement, a course which Morton has refused to take. Pecora also suggested last week that such hearings would be a "circus" and may interfere with more thoughtful analyses of the statement. Recourse to the courts is thus a very likely possibility for environmentalist groups, and it may well be that construction will be delayed at least until 1973. In that case, a full analysis of the trans-Canada alternative may yet be completed before construction starts in Alaska.

NEWS AND VIEWS

Anatomy of Lunar Magic

As far as petrologists were concerned, the National Aeronautics and Space Administration programme for the investigation of lunar rocks could hardly have been better timed. In the early 1960s petrologists had acquired a new tool, the electron microprobe, comparable in importance to the hammer and the polarizing microscope. By July 1969, when the Apollo 11 mission returned, most of the teething troubles of the new instruments had been overcome; the precious nature of the lunar samples, the fine size of the grains, extreme textural disequilibrium and the need to obtain results quickly all combined to demonstrate the power of this analytical method. Within a few months of the samples being collected, the essential features of the crystallization path of lunar basalts had been established: early growth of magnesium-rich olivine and pyroxenes, oxide phases and calcic plagioclase results in extreme iron enrichment of the remaining liquid which precipitates small quantities of a sulphide liquid and a siliceous, potassium-rich liquid.

In the immiscible "granitic" liquid are concentrated potassium, rubidium, thorium and uranium, the long-lived isotopes of which are a vital aid in understanding the chronology and heat budget of the Moon. Also concentrated in this liquid are a group of trace elements, including barium, yttrium, rare earths, zirconium, hafnium, phosphorus and niobium, about which are centred many of the geochemical arguments concerning the differences between terrestrial and lunar rocks. Humorists at the California Institute of Technology have coined the names KREEP and Magic Component for material rich in these trace elements. Clearly, a knowledge of the petrology of the "potassic granite" material is of importance in understanding how it is produced and where it is likely to be found on the Moon elsewhere than in the basalts.

Here again, the electron microprobe is proving its great value; on page 215 of this issue of *Nature* Professor G. M. Brown's lunar team at the University of Durham report the discovery of two new zirconium-rich phases and review the mineralogy of Zr-Ti-Fe oxides found in the lunar granitic material. The most abundant zirconium-rich phase in the lunar basalts is the recently discovered mineral tranquillityite (type locality: the Sea of Tranquillity) which contains about 15 per cent SiO_2 in addition to large amounts of FeO , TiO_2 and ZrO_2 and lesser amounts of Y_2O_3 and rare earth elements. Before the discovery of tranquillityite, the potassium-rich mineral whitlockite was the only identified carrier of rare earth elements in more than trace amounts; enrichment of rare earths in another group of lunar minerals, with a potentially different stability range, increases the possibilities for using this group of elements in interpreting the Moon's petrogenesis.

Peckett *et al.*'s new phases "X" and the aptly called yttrium-rich phase "Y" are essentially silica free, as are other Fe-Ti-Zr oxides reported by other investigators. The

appearance of zirconian SiO_2 -free minerals in the granitic fraction is rather strange, for terrestrial granitic rocks invariably contain zirconium as the silicate ZrSiO_4 , and baddeleyite, ZrO_2 , and the compound oxide zirkelite are restricted to rocks in which silica activity is very low indeed. These last rocks lie at the end of an evolutionary process in which sodium is often enriched in the residual liquids making them strongly alkalic. The puzzling paucity of sodium in lunar rocks tends to obscure the fact that their geochemistry otherwise shares more aspects with terrestrial alkalic than tholeiitic rocks; it is possible that the sodium deficiency of the lunar surface rocks can be attributed to a loss of vapour at the time of eruption.

As Peckett *et al.* stress, the petrogenetic value of their work will only be realized by experiments of the stability relations of the newly identified minerals; certainly the analytical work has posed the problems and suggests a chemical system suitable for their investigation.—From a Correspondent.

Infrared Spectra and DNA

COMPARED with the wide application of optical spectroscopic techniques (ultraviolet, optical rotatory dispersion and circular dichroism), infrared spectroscopy has been little used in physical biochemistry, probably because in the early days of the technique the acquisition of infrared spectra was considerably more difficult than for the visible and ultraviolet region of the spectrum. Furthermore, it is difficult to work with dilute aqueous solutions because of the absorption of the solvent. Nevertheless, unlike the optical region, the infrared spectrum contains many absorption bands and in theory the technique is capable of giving detailed information.

With improvements in reliability and reproducibility of infrared spectrometers which allow the accurate monitoring of changes in spectra, there has recently been an increase in the application of the technique to molecular biophysics. This aspect was demonstrated several years ago by H. Todd Miles and his colleagues (for example, S. C. Howard *et al.*, *J. Mol. Biol.*, **16**, 415; 1966), who monitored the changes in intensities of infrared bands characteristic of different helical conformations of synthetic polyribonucleotides with themselves and with purine nucleosides and nucleotides. A recent prominent defector from the short wavelength region of the spectrum is J. Brahms, who is well known for his contributions to circular dichroism studies of oligonucleotides, polynucleotides and nucleic acids. Brahms and his colleague Pilet have used polarized infrared spectroscopy to follow the B $\rightarrow$ A transition in sodium salts of DNA (*Nature New Biology*, **236**, 99; 1972).

Polarized infrared spectroscopy is a powerful technique for obtaining information on the conformation of poly-

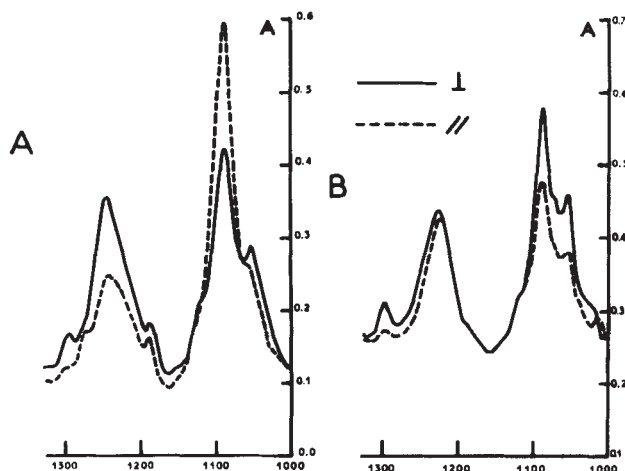
meric systems with fibre type orientation, that is, extended chains or uniform helices oriented with the long axis aligned in one direction. The orientation can either be naturally occurring as in silks, collagen fibrils, keratin and the like, or can be induced by stretching films or by shearing viscous solutions. In these ordered systems the basic repeat unit of the polymer—the amide group of a polypeptide chain or the nucleotide of a polynucleotide—will have a regular orientation with respect to the fibre axis. It follows that the transition moments of infrared vibrations located in these repeat units will also be regularly oriented and an estimation of their angles of orientation can be obtained from the dichroic nature of their infrared absorption bands. The dichroic effects are obtained by comparing two spectra recorded with the electric vector of the polarized infrared radiation either parallel or perpendicular to the axis of orientation.

For polymeric systems X-ray diffraction patterns contain limited information and the data obtained from infrared dichroic spectra are often of considerable value in deciding between different conformations allowable by the diffraction of the fibre; for example, although the position of the phosphate groups of DNA can be defined to within 0.3 Å, the X-ray data are relatively insensitive “to small rotations on the group about its centre” (Fuller *et al.*, *J. Mol. Biol.*, **12**, 60; 1965) and the orientation of the phosphate group is different in each of the successive models proposed for the B form of DNA.

Attempts have been made to correlate the orientation of the phosphate group with the polarized infrared data but whereas the earlier workers were in agreement on the infrared data for the B form of DNA there were doubts as to whether the A form had been fully characterized (M. Tsuboi, *Applied Spectroscopy Reviews*, **3**, 45, Dekker, 1970). With the present knowledge of the role of salts in the B→A transition of sodium DNA, Pilet and Brahms have now resolved these difficulties and have obtained clear infrared evidence for the transition. The figure here (provided by Dr Brahms) shows the dichroic bands of the phosphate group vibration for the B and A forms of sodium DNA. The full and broken lines are for the E-vector perpendicular and are parallel to the direction of orientation respectively. The band at $1,230\text{ cm}^{-1}$ is assigned to the antisymmetrical stretching vibration of the PO_2^- group with its transition moment directed along the O . . . O line. The band corresponding to the symmetrical stretching vibration of this group is at $1,090\text{ cm}^{-1}$ with transition moment along the OPO bisector.

As can be seen there are striking differences in the dichroisms of these bands in the two spectra which demonstrate considerably different orientations of the phosphate group for the two forms. From the dichroisms of these bands the orientation of the phosphate group with respect to the helix axis can be estimated. For the A form these orientations are 65° for the O . . . O line and 45° for the OPO bisector. The corresponding angles from the X-ray structure of the A form (Fuller *et al.*) are 65° and 49° which are in better agreement with the infrared figures than for the refined model of Arnott *et al.* (*Acta Crystallogr.*, **B25**, 2292; 1969) which gives 65° and 31° respectively. For the B form the infrared data give angles of 55° for the O . . . O line and 70° for the OPO bisector and the corresponding angles from Arnott's refined model of this form are 61° and 70° .

With these results of Pilet and Brahms there is now



Dichroic bands of the phosphate group vibration for the B and A forms of sodium DNA.

almost complete agreement between the X-ray diffraction and polarized infrared results for all the fibre structures of RNA and DNA. The value of this new work, however, is to be found not only in clearing up the ambiguity concerning the A form of DNA but also in the confidence with which the infrared technique can now be applied to the study of DNA conformations and changes of conformations in more complex systems. There is, for example, considerable interest in whether histones or histone fragments modify the structure of DNA as suggested by circular dichroism and optical rotatory dispersion studies of histone/DNA complexes.

The striking differences in the polarized infrared spectra of the A and B forms of DNA encourage optimism that any significant modification of these conformations by an interacting system would be readily detected. But small modifications which give, for example, what might be called a family of B forms and so forth would probably be very difficult to follow. The technique has particular application to these complex systems, because, in general, they are far less crystalline than pure DNA and their X-ray patterns are often very diffuse. These comments apply, of course, not only to proteins, but also to any agent which modifies the structure of DNA.—E. M. B.

“The Elephant”

WHEN one has been reading a Greek doctor's notes on the causes and treatment of various maladies—epilepsy, tetanus, satyriasis and so forth—it comes as rather a shock to find a section headed “The Elephant”, which begins with a description of the animal. It is not surprising therefore that most people who have written about the elephant have passed over what Aretaeus had to say in the second century AD. For interest's sake, and for one or two rather fetching similes, here is an abridged version of his remarks taken from *Corpus Medicorum Craecorum* (edit. by K. Hude, **2**, *Aretaeus*, Book 4, Ch. 13, Sections 1–7; Leipzig, 1923).

The elephant is very big and thick skinned. He is as big as a siege tower and dark all over. Other animals vary in colour but elephants are dark and murky, like night and death. He has no markings anywhere on his body. His neck appears to be very small, his ears big

and broad like wings, reaching as far as the collar bone and chest, concealing the neck rather like the sails of a ship. His tusks are amazing; they are very white and stand out against the animal's very dark colouring. Some people call them "teeth". These tusks are not on the forehead or by the temples as they are in other animals, but grow by the mouth and upper jaw. Nor do they stick straight out, but curve gently upwards. In elephants of medium size the tusks are the length of one's outstretched arm, but in others they can be almost twice as long.

The trunk is held well away from the mouth and is boneless and winding, like a snake. It has two holes in the end and these go right through, almost to the lungs, like a double pipe. This pipe enables the elephant to breathe, as through a nose. He uses it like a pair of hands or a beaker as well. It can grip things very powerfully and nobody can release anything from it, unless he be a stronger elephant. The elephant uses it to search out grass which he does not eat directly from the ground with his mouth. His legs lift him well off the ground, so he cannot forage with his mouth; his tusks also prevent him from doing this. So he gathers up a great bundle with his trunk, like someone binding a sheaf of wheat, and shoves it into his stomach. Our ancestors did well to call this the proboscis.

He cannot drink straight from a pool or stream, either. If he is thirsty, he first dips the end of his nose in the water, then, just as though he were taking a deep breath, sucks up a lot of water; and when he has filled his nose full, like a drinking horn, he pours the stream into his mouth. Then he repeats the process, just as though his stomach were a ship taking on cargo. The hide is rough and thick, full of mounds and clefts which are long, deep and hollow, and run off each other at all sorts of angles, so that the whole skin looks like a thrice-ploughed field. Other creatures have long, flowing hair; that of the elephant is short and soft. He differs in many other ways, too, bending at the knee like a man, having breasts near the armpit like a woman. . . .

At this point, irritatingly, Aretaeus breaks off and begins to discuss elephantiasis which, of course, was the point of his preliminary description.—From a Correspondent.

PROTEINS

Native at Nativity

from our Molecular Biology Correspondent

IN spite of all that is now known about the process by which a polypeptide chain finds its way into its native, biologically functional, conformation, the events between polymerization of the amino-acids on the ribosome and the appearance of the conformationally recognizable article are still essentially *terra incognita*. A few landmarks can, it is true, be discerned. Some cases are documented in which the C-terminal end of the chain is indispensable for folding, or biological activity, and, because peptide synthesis proceeds from the N-terminus, this makes it seem that there can be no folding until the chain is complete, or nearly so. On the other hand, antigenic reactivity has been recognized in apparently incomplete protein chains, and it has been reported that antibodies possess activity when one of their constituent chains is still being run off the ribosome. There is also some fragmentary evidence in other cases about the formation of disulphide bonds only after completion of the chain, and also of failure of subunit enzymes to refold in the presence of extraneous proteins, such as might be present in the cellular milieu at synthesis. An interesting contribution to the problem comes from Hamlin and Zabin (*Proc. US Nat. Acad. Sci.*, **69**, 412; 1972), who have examined the development of antigenic activity in β -galactosidase in the course of synthesis.

In the first place, the annihilation of antigenic activity by denaturing procedures, such as heating or exposure to detergent, may be taken as evidence that the antigenicity is a property of the native conformation, or at least some facets of it. Reactivity towards antibodies to β -galactosidase was found in the ribosome fraction of a strain of *Escherichia coli* producing high concentrations of the enzyme; the binding of antibodies to ribosomes from a deletion mutant strain was an order of magnitude lower. When puromycin was introduced into the cell lysate to effect release of the partly formed chains from the ribosomes, antigenic activity appeared in the supernatant.

The fraction of ribosomes bearing incomplete β -galactosidase chains was estimated by a curious and original procedure. Evidently β -galactosidase is an enzyme that can be put together non-covalently, but in working order, from two fragments: one of these is a segment from the N-terminal end, and can be isolated by cyanogen bromide cleavage. Now a deletion mutant is available in which this part of the chain is not synthesized, and this defective product gives rise to activity only when

mixed with the cyanogen bromide fragment. When now the ribosomes were treated with this reagent to generate the fragment, the enzymatic activity appearing on addition of the complementing peptide led to an estimate of one partial β -galactosidase chain on about one in five ribosomes. When synthesis of β -galactosidase was induced with a substrate analogue, the appearance of the cyanogen bromide fragment is observed after 20–30 s, and the concentration of nascent chains is still increasing at 90 s, although no completed chains are released up to this time, as shown by the absence of enzymatic activity.

The β -galactosidase chain is a long one, and it seems as though parts of it (like, for example, those of an immunoglobulin chain refolding *in vitro*) may independently assume characteristic folded conformations, which correspond to the antigenic sites.

The future in the cell of incomplete or incorrect polypeptide chains is evidently bleak, for Goldberg (*ibid.*, 422) has shown that they are catabolically eliminated with great despatch. Degradation in *E. coli* was measured by the appearance of free radioactive amino-acids at given time after administration of a pulse label. Any seriously aberrant proteins seem to be treated in the same way by the degradative machinery. The rate of overall breakdown in a mutant characterized by defective ribosomes, that lead to a greatly increased number of translation errors, is several times faster than in wild type or revertant cells. The effect is the same when the incomplete chains in normal cells are released with puromycin, and there are also striking increases in degradation rates in cells grown in the presence of analogues of natural amino-acids, as also noted by earlier workers.

Different analogues, however, differ in the extent to which they elicit this response, and there seems to be a good correlation between a rapid rate of polypeptide degradation and lethal effect on the cell. One might surmise that analogues with side chains that do not readily fit into their slot in a protein structure will produce functionally still-born enzymes, so that the cell will die, and that these will by the same token be readily degradable. At all events it seems probable that proteases exist in the cell which have the express function of eliminating undesirable polypeptide material, and that this last can be equated with chains that for one reason or another do not fold into the tight globular conformations characteristic of native enzymes. This affords reinforcement for the view that in general the native conformation does indeed demand the whole length of the chain. The vulnerability of denatured proteins, or random polypeptide chains in

general, to proteolysis is, of course, a long-established principle.

It may be noted that normal proteins are also catabolized, though slowly, in cells in stationary phase, presumably to provide an amino-acid pool for the next bout of synthesis. The process of eliminating defective proteins occurs with equal efficiency in growing and stationary cells, and may be subject to a quite different mode of control. The suppression of the degradation process by oxidative phosphorylation inhibitors suggests that it may involve an energy-consuming ATP-regulated step.

CONSERVATION

Reconstructing Nature

from a Correspondent

THE terms conservation and preservation were for long virtually synonymous in the minds of British ecologists, but recently it has become increasingly recognized that conservation must be an active rather than a passive process. This shift in ecological thinking is partially the consequence of the recognition of the impact of man on the environment and also of the realization that nature untended can produce a uniformity of habitat which man finds uninteresting. Thus conservation has come to mean management and management presupposes a value judgment as to the direction in which control is to be exercised.

The desires and aims which underlie management programmes are varied; often they seek environmental stability, sometimes high productivity. In the nature reserves of Britain, however, one high priority has been the maintenance of species diversity, which in turn implies habitat diversity. In the current issue of *Biological Conservation* (4, 135; 1972) M. Rawes and D. Welch of the Nature Conservancy describe some experiments concerned with increasing floristic diversity on the Moor House National Nature Reserve in Westmorland.

This upland area, in common with most hill regions of Britain, is poor in plant species, a poverty which may well have resulted from centuries of heavy grazing by sheep and cattle. A further problem is that many plant species which seem to be potentially capable of survival under such conditions are now extinct in the area. In order to see if there was a relation between grazing and the paucity of plant species at Moor House, sample plots which excluded grazing animals from the vegetation on a variety of soil types were set up fifteen years ago. Several upland plant species which now have restricted distributions were also introduced into the "enclosures". A recent survey of these

plots, now reported by Rawes and Welch, shows that many of the introduced mountain plants thrive at Moor House in the absence of grazing, suggesting that their demise may well have been caused by domestic animals. Other plants, however, have failed to establish themselves because of competition from coarse grasses and sedges which have also benefited from the lack of grazing.

Fifteen years is a relatively short time in terms of the development and maturation of an ecosystem and it is possible that more species will be eliminated as climax vegetation is achieved. At present it is not known what this climax will be in the absence of sheep, but it is likely that either dwarf shrubs or coarse herbs will assume dominance and this could lead to further extinctions among the introduced species.

Besides the interest of this work in reconstructing the "natural" vegetation of the North Pennines, it brings to the fore the question of policy in reserve management. By the local exclusion of grazing and the introduction of a flora from another geographical region, habitats can be diversified and both the attractiveness and the interest of a nature reserve are thus increased. But should this be the highest aim? Having accepted man's obligation actively to manage reserves, should limits be set to the extent of his biotic manipulations?

The value judgments demanded by these questions are fundamental to the concept of conservation.

Enzyme of a Superphage

THE bacteriophage PM2 which lives on pseudomonads may not yet be as familiar to the spectators and practitioners of molecular biology as QB, R17, T4 and the other coliphages, but there is every reason to think that it soon will be. PM2 seems to have more or less everything a molecular biologist could ask for: it consists of a covalently circular, double stranded DNA molecule in an icosahedral particle with four species of polypeptide, one of which is a glycoprotein and, most importantly with an internal lipid bilayer, a membrane.

In short, PM2 is a bacteriophage which has many of the structural features of the enveloped viruses which infect animal cells, and as Datta and Franklin report in next Wednesday's *Nature New Biology* (April 5), like the enveloped animal viruses, PM2 phage particles apparently contain a nucleic acid polymerase activity.

According to Datta and Franklin, when highly purified PM2 particles are

PALAEOHYDROLOGY

History of the Black Sea

STUDIES of the distribution of oxygen and isotopes in organic matter from a sediment core suggest that the Black Sea was a brackish freshwater lake up until 9,000 years ago. The core (15 × 15 × 600 cm), one of several collected during the cruise of RV Atlantis in the spring of 1969, has been analysed at Woods Hole Oceanographic Institution by R. G. Deuser, who has found that it covers the past 17,000 years of the sedimentary history of the Black Sea (*J. Geophys. Res.*, 77, 1071; 1972).

The core, like others from the Black Sea, is divided into three easily recognizable layers: first, a series of alternating thin light and dark layers of high carbonate content (coccolith ooze); second, a dark region rich in organic matter (called sapropel); and at the bottom a series of light and dark bands containing rather less carbonate and organic material (lutite). The beginning of the top zone is dated at 3,000 yr BP, and that of the middle zone at 17,000 yr BP. But why were there abrupt changes in the type of sediment being laid down at these dates?

Deuser has tackled this problem by analysing $^{18}\text{O}/^{16}\text{O}$ and $^{13}\text{C}/^{12}\text{C}$ ratios throughout the core. In carbonate samples, the ratio of oxygen isotopes is roughly constant except in the upper 1.5 m of the core, above which there is a very rapid increase of ^{18}O . Carbon isotope ratios from the same carbonates show a more complex variation with

exposed to a non-ionic detergent, an essential step, and then incubated in a polymerase assay medium containing Mn^{2+} and the four ribonucleoside triphosphates an acid precipitable RNA is made. The synthesis of this RNA is blocked by incubating the disrupted phage particles with DNAase which indicates the phage DNA is the template from which the RNA is transcribed; the polymerase activity chromatographs with the PM2 phage particles.

The relationship between the RNA made by the phage polymerase and the phage DNA has yet to be established by hybridization experiments. Likewise the origin of the polymerase, whether it is a bacterial rather than a virus-coded enzyme, has still to be determined as has its function during the phage's replicative cycle. But that PM2 particles contain, internally, a DNA dependent RNA polymerase seems beyond dispute, and the parallels between this phage and the enveloped animal viruses become even more striking.

depth, and there are pronounced discontinuities at depths of 1 m, 1.8 m and 3 m. Sediments rich in organic carbon, between 18 cm and 67 cm and between 76 cm and 83 cm, also show short period fluctuations in $^{13}\text{C}/^{12}\text{C}$, but with an overall trend towards ^{13}C enrichment in the younger samples.

Deuser believes that the uniformity of ^{18}O content in most of the core arises as a result of redeposition, mixing and ion exchange. By comparison, the exchange of carbon isotopes would take place more slowly, because in the carbonate carbon can only be exchanged together with the coordinated oxygen atoms, whereas single oxygen atoms can exchange without affecting the carbon. So the carbon profiles probably provide the more accurate detailed history of changes affecting the Black Sea, although the oxygen evidence clearly points to a dramatic change in conditions beginning roughly 9,000 yr BP.

Salinity changes are, of course, an obvious principal cause of changes in the isotope balance. From the isotope evidence and other studies of sedimentary changes a picture of the history of the Black Sea since the most recent glaciation now emerges. For some time before 17,000 yr BP until 9,000 yr BP the "sea" was a freshwater lake isolated from the world's oceans. Rather than salt water entering from the Mediterranean, there may have been spillage of freshwater from the lake across the Bosphorus from time to time. From roughly 15,000 yr BP the worldwide sea level began to rise (J. D. Milliman and K. O. Emery, *Science*, **162**, 1121; 1968) and reached the level of the Bosphorus sill roughly 9,000 yr BP. Salinity then built up in the Black Sea until present day levels were reached, roughly 3,000 years ago, and the sea has now settled down to a stable salinity level.

CEN X-3

Peculiar Binary

by our Cosmology Correspondent

THE binary nature of Cen X-3 seems to have been confirmed, and details of the structure of the individual components of the system are now emerging. E. Schreier and colleagues of American Science and Engineering Inc. have now reported an analysis of data on this source which are the result of a year's observations from the Uhuru satellite (*Astrophys. J. Lett.*, **172**, L79; 1972). As well as the 4.8 s pulsation period found earlier, it is now clear that Cen X-3 changes in a regular way over a period of about 2 days, and that the exact period of the ~ 4.8 s variation is affected by this second regular change in intensity.

From the data covering 1971 the AS&E group have found that the source

can appear at either of two levels of intensity, and that the transition between these levels takes roughly one hour. In May 1971 they were able to obtain a continuous, detailed set of observations over a period of one week. With these data as a guide, they have been able to pick out the regular ~ 2 day period for the variations between the two states throughout the year's data. The 4.8 s period itself is subject to variations of about 0.02 s on successive days. The average period is 4.842 s and usually the period is between 4.832 s and 4.853 s. Overall, Schreier and colleagues summarize their observations as evidence that:

- Two distinct average intensity levels differ by a factor of ten and repeat with a period of 2.08710 ± 0.00015 day.
- The low level sometimes persists for several days, but the high level is never found when the low level is predicted.
- The 4.842 s period shows a sinusoidal variation of period with null points of the variation coinciding with the centres of the high and low states of intensity to within 0.003 ± 0.006 day.

This evidence points to an occulting binary system in which the short period pulsations come from a compact object orbiting a much larger object. The variations in the ~ 4.8 s period can then be interpreted as a result of the Doppler

effect. Because the object associated with the intense X-ray emission must be very small on any conventional understanding of the mechanism causing the pulsations its mass is probably no more than $1 M_{\odot}$, which suggests that the companion is a giant with mass between $17 M_{\odot}$ and $46 M_{\odot}$. But although a massive main sequence star or a B0 supergiant seems a suitable candidate for the central object on the face of the mass and radius requirements, the possibility remains that a more compact object with an extended atmosphere could also fill the role.

These observations are bound to stimulate further optical surveys of the region—Cen X-3 is now known to lie at RA 11 hr 19 m ± 0.4 m, dec. $-60^{\circ} 19' 2 \pm 3'$ —but Schreier and his colleagues caution that the system is probably dominated optically by the central massive object, and that it is unlikely that either of the two periods reported will be detected photometrically.

This work suggests that there may be a class of X-ray sources which are associated with binary systems. It has already been shown that the X-ray source Cyg X-1 is a binary system with a period of 5.6 days and there is also evidence which indicates that a pulsating X-ray source in Hercules also shows two intensity levels which resemble those shown by Cen X-3.

More about RD 114 Cells

IF any C-type RNA virus remains longer than a few months in the list of contenders for the dubious distinction of being the first human RNA tumour virus to be discovered it is time to start to take the claim seriously. So many people are intent on finding human RNA cancer viruses homologous to the sarcoma and leukaemia viruses in lower mammals and birds that every suspect virus is immediately and extensively screened by competing research groups. Usually the particular virus is quickly eliminated by being shown to be a contaminating animal virus, but one putative human cancer virus, the so-called RD 114 virus, has withstood such testing for the past several months. It really seems that RD 114 virus may have a human origin and information about the lineage of the RD 114 cells which liberate the virus, such as that reported by Nelson-Rees, McAllister and Gardner in next Wednesday's *Nature New Biology* (April 5), assumes considerable importance.

The viruses which liberate the RD 114 cells isolated by McAllister and his colleagues have an unusual history. They were obtained as direct outgrowths when a piece of a solitary rhabdomyosarcoma taken from the brain of a kitten was placed in culture.

Some 78 days earlier the kitten, then a foetus, had been injected with a line of human rhabdomyosarcoma cells called RD 2 cells. These RD 2 cells do not produce a C-type virus but the RD 114 cells do. Initially everybody anticipated that the human cells had picked up a feline leukaemia virus during passage in the kitten. Repeated and diverse tests aimed at showing that the RD 114 virus is a cat virus have, however, failed and the possibility remains that the virus has a human origin.

So much for RD 114 virus but what about the RD 114 cells themselves? Can one be sure they are human cells and not cat cells? The analyses of the chromosomal constitutions of populations of RD 2 cells and RD 114 cells reported by Nelson-Rees *et al.* establish beyond doubt that the RD 114 cells are human cells. Moreover, the presence of a ring marker chromosome in about 70–80 per cent of RD 114 cells but only about 10 per cent of RD 2 cells can be interpreted as evidence that the brain tumour from which the RD 114 cells were isolated arose from the proliferation of just one or a few of the inoculated RD 2 cells. In other words the tumour from which RD 114 cells were isolated may have been a clone from one RD 2 cell.

TERPENE BIOSYNTHESIS

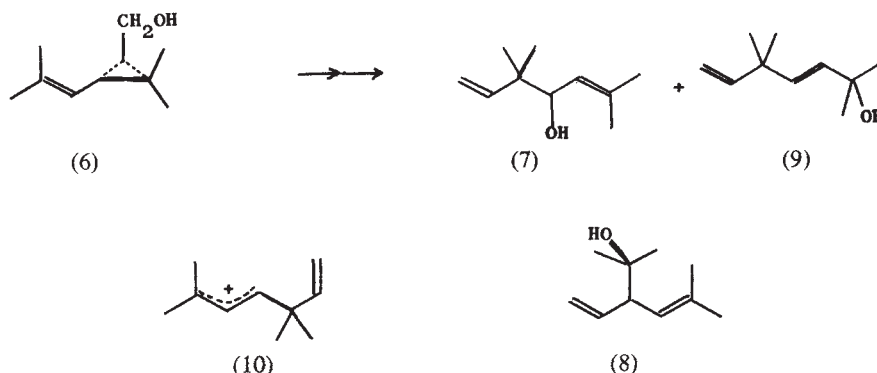
Chains, Triangles and Squares

from our Biological Chemistry Correspondent

J. W. CORNFORTH and his collaborators have managed to solve most of the secrets of farnesol pyrophosphate biosynthesis and its conversion into squalene. The source and stereochemistry of all fifty hydrogens in squalene are known, excepting only the methyl hydrogens at the ends of the chain. This last problem, more severe than the rest, requires the power to discriminate between three equivalent hydrogens bonded to the same carbon. Of late, both Cornforth and Arigoni have developed techniques for the solution of this problem, based on the chemical synthesis of CH_3 -groups containing one atom each of the three hydrogen isotopes, protium, deuterium and tritium, in a defined array which can be identified by an enzymatic assay.

Cornforth has now applied this method to resolve the nature of hydrogen transfers in the isomerization of 3-methyl-3-butenyl pyrophosphate (1) into 3-methyl-2-butenyl pyrophosphate (2) (*Chem. Comm.*, **1971**, 1599). The enzyme isopentenyl pyrophosphate isomerase removes the 2-*pro-R*-hydrogen (H^*) from (1) and a proton is supplied from the medium to the upper (*re*) side of (2) which, by suitable choice of isotopes, contains a methyl group with protium, deuterium and tritium. The stereochemical relation of incoming and outgoing hydrogens in the isomerization suggests a concerted addition-abstraction process.

The hypothesis which is currently in favour for the conversion of farnesyl pyrophosphate into squalene involves presqualene pyrophosphate (see *Nature*, **230**, 429; 1971) though in the past there has been some disagreement about its structure. This is largely resolved by Popják's revision of his structure for presqualene pyrophosphate to accord with that of Rilling in the light of new and refined data (*J. Biol. Chem.*, **246**,



6254; 1971). Most groups have their own hypothesis for its conversion into squalene: Popják's novelty is the transformation of the cyclopropylcarbinyl system (3) into a cyclobutane derivative (4) *en route* to the linear squalene chain (5).

An important feature of the natural terpenes is the regular head-to-tail linkage produced by the addition of (1) to (2). There is something peculiar about daisies (Cpositae) which provide an apparently exclusive source of anomalous skeletal types including chrysanthemyl (6), artemisyl (7) and santolinyl (8) monoterpenes. The obvious genetic link plus particular chemical considerations has been an inspiration for several model studies which Poulter has now capped (*Tetrahedron Lett.*, **1972**, 69, 71) by demonstrating the production of santolina alcohol (8) from chrysanthemyl alcohol (6) with the correct stereochemical correlation. Because compounds of the artemisyl group, yomogi (9) and artemisia (7) alcohols, are formed at the same time, it seems plausible that a common precursor, also related to presqualene pyrophosphate, features in the biosynthesis of the diverse monoterpene types of the daisy family.

The chemistry of these processes

hinges around a common cation, very probably of the non-classical type which is well known to interrelate cyclobutyl, cyclopropylcarbinyl and

homoallyl systems, represented here as (10). The dying embers of heatedly discussed hypotheses invoking sulphonium ylides in squalene biogenesis have been stirred by Barry Trost (*Chem. Comm.*, **1971**, 1639). His group show that the formation of (7) from (6) can be reversed by solvolysis of the sulphonium salt derived from artemisia thiol (7; $\text{O}=\text{S}$). Although this reaction gives largely yomogi-type product (9), small but highly significant amounts of santolina (8) and chrysanthemyl (6) compounds are produced and also the head-to-head linked monoterpene of the squalene type ((5); $\text{R}=\text{Me}$, $^*\text{H}=\text{OMe}$).

Perhaps, after all, the biosynthesis of squalene does involve sulphonium ylide rearrangements which furnish a cation inside the enzymatic site that is normally reduced to squalene (5) but, in the absence of NADPH, is trapped by pyrophosphate with a different regio-specificity to yield "presqualene" pyrophosphate.

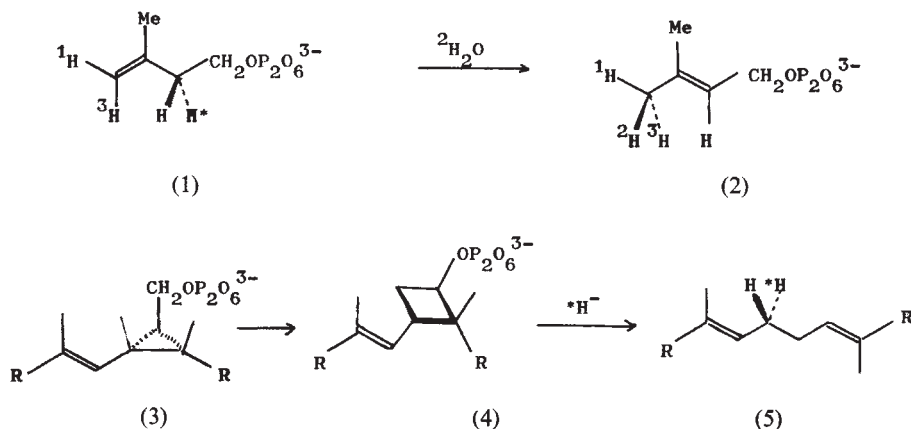
GLASS

Phase Separation

from our Materials Science Correspondent

WITH the growing application of transmission electron microscopy and small-angle X-ray scattering to the examination of glasses, it has come to be recognized that the existence of miscibility gaps in the constitutional diagrams of glasses is quite common. Glass-in-glass phase separation during cooling is now seen to be the rule rather than the exception, and this has important implications for the understanding and control of devitrification. But although much effort has gone into the investigation of phase separation in glasses, by the fore-mentioned techniques especially, scarcely anything is known of the actual form of the miscibility gaps in specific glass systems.

This lack is now beginning to be



rectified. An impressive new investigation by two Japanese industrial scientists (K. Nakagawa and T. Izumitani, *J. Non-Crystall. Solids*, 7, 168; 1972) has served to determine the form of part of the miscibility gap in the $\text{Li}_2\text{O}-\text{Al}_2\text{O}_3-\text{SiO}_2$ system, which is of great importance for the production of glass ceramics with minimum thermal expansion. This study is at the same time an illustration of the power of that very simple technique, the determination of lattice parameters from X-ray diffraction patterns. Nakagawa and Izumitani prepared two series of glasses along ternary sections of constant $\text{Li}_2\text{O}/\text{Al}_2\text{O}_3$ ratio, and heat-treated them for different times at several temperatures to crystallize them (with the help of dissolved TiO_2 or ZrO_2 catalyst). The crystallized phase was always a ternary solid solution: the *a* and *c* lattice parameters varied as the phase ranged from nearly pure β -quartz to β -eucryptite, $\text{Li}_2\text{O} \cdot \text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2$.

Isothermal heat treatments of a range of glasses at different temperatures produced classical plots of lattice parameter versus silica content, with horizontal plateaux identifying the region in which the crystalline phase is of constant composition. Such fields lie inside the miscibility gap. The crystalline phase was taken to crystallize at the same composition as one of the coexistent glassy phases (an assumption which strictly requires confirmation).

Examination of the lattice parameters of the phase at a range of temperatures proved that it had crystallized out of the silica-poor phase, and accordingly the form of the miscibility gap on the silica-poor side was accurately determined. (The peak of the gap lies at 800–820° C and about 85 wt per cent silica.) The silica-rich glassy phase does not crystallize and remains in the final glass ceramic. The fraction of residual glassy phase was determined as a function of temperature and could have been (but was not) used to determine the silica-rich side of the miscibility gap. The conclusions from X-ray study were tested and confirmed by electron-micrographic observations.

Another original approach to the problem of determining some features of a miscibility gap was recently described by C. T. Moynihan, P. B. Macedo, I. D. Aggarwal and W. E. Schnaus of the Catholic University of America at Washington (*ibid.*, 6, 322; 1971). They performed differential calorimetric scans on cooling various glasses in the Pb-Ge-As-Se system. The scans showed two discontinuities which they were able to identify with the glass-transition temperatures of the two separated glassy phases. A critical analysis of the magnitudes of the specific heat discontinuities for glasses of various macroscopic compositions allowed some points on the miscibility

gap to be located. This arises because the equilibrium begins to be "frozen" as soon as one of the two glassy phases has been cooled to its transition temperature.

TUMOUR VIRUSES

Transforming Subunit

from our Cell Biology Correspondent

THE isolation of mutant strains of Rous sarcoma virus (RSV) which carry temperature sensitive lesions in a gene or genes the expression of which is required to transform chick fibroblasts rules out the possibility that viral transformation is a hit and run affair. Indeed, quite the reverse is the case, for to keep a fibroblast transformed not only must the viral genome or part of it be maintained in the cell but also it must be continuously expressed; when, for example, a temperature sensitive transforming gene(s) is switched off by raising the temperature the phenotype of the transformed fibroblast reverts to that of an untransformed fibroblast.

Precisely what proteins are specified by the transforming genes of Rous sarcoma virus, and for that matter by the corresponding genes of any other oncogenic virus, is at present an unanswerable question which will probably long reside in the realms of speculation, for there are no obvious short cuts to an unequivocal answer. Looking for viral specified transforming proteins in a morass of cell proteins is, if not hopeless, daunting enough to dissuade most experimenters. If, however, what Duesberg and Martin have to say in the current issue of *Virology* (47, 494; 1972) can be taken at face value, and there is no good reason for doing otherwise, it should not be long before that part of the Rous sarcoma virus genome which contains at least some of the transforming genes is, in useful amounts, separated from the part carrying genes not involved in transformation of fibroblasts.

As Duesberg has shown, the subunit RNA molecules obtained when the 60–70S single-stranded genomic RNA of avian sarcoma viruses is denatured either by heat or by DMSO can be separated into two size classes by polyacrylamide gel electrophoresis—so-called *a* subunits with a larger molecular weight than *b* subunits. When, by contrast, genomic RNA of avian leukosis virus, which cannot transform fibroblasts, or of a non-transforming variant of the B77 strain of Rous sarcoma virus is similarly denatured and analysed, Duesberg finds only *b* subunits. One attractive way to account for these observations is to suggest that *a* subunits contain the genes that are essential for the transformation of fibroblasts; but one might equally

suggest that *a* subunit RNA is only made in transformed cells and therefore only appears in those viruses which have replicated in transformed cells.

It is this possibility which Martin and Duesberg have now eliminated by analysing the subunit composition of the RNA of a temperature sensitive mutant, T5, of Schmidt Rupp RSV isolated by Martin, and of stocks of Bryan high titre RSV. Martin's mutant replicates in chick fibroblasts at 41° C but cannot transform cells at that temperature although virus produced at 41° C can transform fibroblasts at 37° C. In other words, T5 carries a temperature sensitive mutation in a transforming gene(s) and if the *a* subunit of RSV RNA carries this gene(s) then *a* subunits should be present in the genomic RNA of T5 virus particles grown in a cell which, at 41° C, has the untransformed-cell phenotype. If, by contrast, the *a* subunit is only found in viruses grown on cells with the transformed-cell phenotype, T5 virus grown in fibroblasts at 41° C should lack *a* subunits. In fact, of course, the T5 virus has *a* subunit RNA irrespective of the temperature at which the virus is grown. What is more, stocks of Bryan high titre sarcoma virus which are known to contain an excess of leukosis virus mixed with a small proportion of sarcoma genomes yield very few *a* subunit RNA molecules, and when by repeated passage non-transforming variants of RSV are produced these virus particles are found to lack *a* subunits.

All these data are consistent with the notion that *a* subunits carry the genes necessary for the transformation of fibroblasts; they also are consistent with the suggestion that the subunits of the sarcoma virus genome may replicate independently as do the RNA subunits of the genomes of flu virus and reovirus.

Duesberg and his colleagues would no doubt predict that FU 19, the temperature sensitive mutant RSV isolated by Biquard and Vigier (*Virology*, 47, 444; 1972), will be found to have *a* subunits, for FU 19 behaves very like Martin's T5 strain. And it seems equally certain that Duesberg and others will soon be attempting to isolate *a* subunits and to discover what genes they carry, perhaps by using them to programme cell free systems which support protein synthesis.

CANCER RESEARCH

Immunological Factors

from a Correspondent

THE possibility of immunological regulation of the growth of malignant cells was discussed by Professor N. A. Mitchison (University College, London) and Professor G. Hamilton Fair-

ley (St Bartholomew's Hospital and Institute of Cancer Research) at the tenth meeting in the series on the principles of experimental and clinical oncology held in the British Museum (Natural History) on March 13. Dr A. J. S. Davies (Institute of Cancer Research) took the chair.

As R. T. Prehn has emphasized (in *Immunological Surveillance*, edit. by R. T. Smith and M. Landy, p. 462, Academic Press, 1970), the popularity of the immunological approach to cancer has varied over the years. At present it is at a high point, first, because of the demonstrations that many tumours have detectable antigenicity both in experimental animals and human beings and, second, because of increased understanding of the cellular basis of immunological responses.

Professor Mitchison said that the available evidence favoured the T (thymus-derived) cell as the most important cellular agent which could be active against malignant cells rather than the B (bursal equivalent or bone marrow-derived) cell. He dealt first with the situation in the tumour-bearing animal. It is possible to demonstrate that lymphocytes bind specifically to antigens but that most of the available methods are for B cells which tend to have greater concentrations of immunoglobulin receptors on their surfaces. Nevertheless there is increasing experimental evidence that T cells can bind specifically to tumour target cell monolayers during prolonged incubation and that this method might in the future provide means of quantitation of specifically reactive T cells in patients with malignancies. B cell quantitation would be possible by various modifications of the Jerne plaque assay and indirect assay of T cell activity could probably be made by quantitation of factors (such as migration inhibition factor) released in the presence of specific antigen.

Studies of inhibition of tumour colony formation *in vitro*, such as those carried out by the Hellströms, probably assayed the activities of both T and B cells, T cells being cytotoxic and the B cells providing anti-tumour antibodies. From the viewpoint of the immunochemist studies of purification of tumour specific antigens were at present unsatisfactory but some progress had been made following the leads of the transplantation immunologists. Perhaps the most promising methods would follow from study of envelope antigens released from virally infected cells and the work of Field and Caspary which shows a cross-reaction between peptides released from tumour cells and encephalitogenic factor.

As far as control mechanisms were concerned, Professor Mitchison stressed

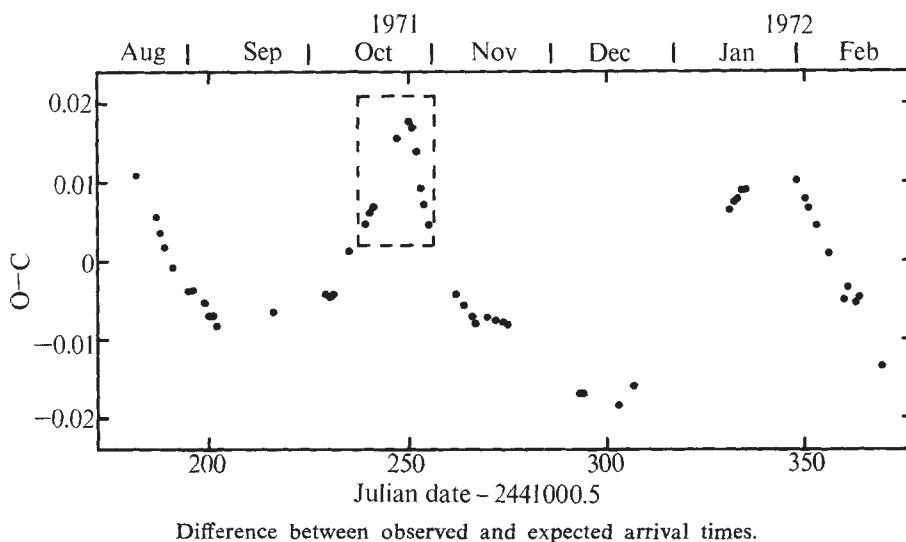
that at present there are interpretative difficulties; for example, in the Hellström-type studies it is difficult to be sure whether an antigen-antibody complex on lymphocytes or on their target cells (or both) prevented destruction of tumours. Nevertheless the principles of selective stimulation of T and B cells are beginning to be understood and they should in the future permit rational manipulation of anti-tumour immunity.

Professor Fairley, as a clinician, said that it was becoming increasingly clear that the situation in man in relation to immunological regulation of tumour growth is similar to that in experimental animals. A clear distinction should be made between chemically and virally induced tumours. In the first there are likely to be individual specific antigens; in the second group specific antigens are present. Attempts at immunotherapy would have to take these differences into account, although at present it was difficult to be sure in man which tumours fell into which

class. Clinical approaches were often hampered by the difficulty of demonstrating anti-tumour activity in the presence of an excess of malignant cells. Nevertheless some progress had been made by comparing the behaviour in mixed lymphocyte cultures of the cells of a patient in remission from acute lymphoblastic leukaemia with cells from the same patient taken and stored at the height of the disease. The evidence suggests that the ostensibly normal cells respond against abnormal blast cells.

Professor Fairley felt strongly that immunotherapeutic attempts were doomed to failure if they were used on patients with full-blown untreated malignancy and that some reduction of the tumour mass by conventional means was an essential prerequisite. The tone of the meeting was hopeful but it seems that it will be some time before there is precise and individual characterization of the immunological relationship between a cancer patient and his tumour.

Crab Pulsar Speeds Up Again



THIS illustration, taken from an article in next Monday's *Nature Physical Science* (April 3), shows that the pulsar in the Crab Nebula is continuing to behave erratically. In particular, the data show that the pulses speeded up during October last year, as they have done before, but this time the speed-up was followed in sufficient detail for it to be clear from a careful analysis that it was not a one-stage process. Rather it seems that the speed-up took place in at least two stages within a time interval of three days around October 26. The speed-up may even have been a continuous process spread over that time interval.

Plotted in the illustration is the differ-

ence between the observed arrival time of the pulses and the arrival time predicted by a least squares fit to the arrival time data. This quantity is plotted in units of the period of the Crab pulsar from August 1971 to February this year.

The data come from optical observations with the 60-cm refracting telescope of the Hamburg Observatory, and are reported by Eckmar Lohsen. They also suggest that the pattern of behaviour of the Crab pulsar after this most recent speed-up was similar to the behaviour after a previous prominent speed-up in September 1969, an observation which will no doubt be further grist to the theorists' mill.

Amorphous Semiconductor Switching

H. K. HENISCH

Materials Research Laboratory, The Pennsylvania State University, University Park, Pennsylvania 16802

Professor Henisch considers amorphous semiconductor switching in the light of the fourth international conference on amorphous and liquid semiconductors held at Ann Arbor in August 1971.

THE subject of switching in amorphous semiconductors is of particular interest at present because of the possibility that switching phenomena might somehow throw new light on the fundamental nature of amorphous matter and because of the appearance of new solid state devices of a kind not feasible with conventional (crystalline) semiconductors. Amorphous semiconductors as such have been known for as long as the crystalline variety but have not caused much excitement (except in the context of xerography) so it is safe to conclude that the new interest in the first aspect owes a great deal to the second. Sentiments widely expressed at a recent international conference¹ bear this out. Nor is this surprising, because new devices and their applications have already become a reality as could be seen from a series of demonstrations by S. R. Ovshinsky (Energy Conversion Devices, Inc.); further new devices are on the horizon (Nicolaidis and Doremus, Hamakawa, Yoshida and Yamanaka, Ovshinsky and Klose); the question is: what becomes of the first aspect? Although many amorphous materials are of interest in this context, I shall limit myself to switching systems based on multi-component chalcogenide glasses, partly for the sake of brevity and partly because only such systems have so far reached the level of practical usefulness.

Characteristics

The principal facts are well known. When thin glass films (1 μm , for example) are placed between non-reactive and non-diffusing electrodes and are examined electrically, their voltage-current characteristics are found to be as shown by the full lines on Fig. 1. The off-state is stable and the on-state metastable, requiring a current of at least I_{MH} (the minimum holding current) for its maintenance. In this form the system is called an ovonic threshold switch. As long as the switching cycle is performed sufficiently fast (for example, at megacycle frequencies), such characteristics are observed for all systems irrespective of glass composition and thus of the glass transition temperature (T_g). In films made of glasses with low T_g , however, the on-state can be stabilized by prolonged power dissipation at the points P_1 or P_2 . The process requires 2 to 15 ms, depending on the applied voltage and series resistance. When such a "set" pulse has been applied, the V - I characteristic in the on-state passes smoothly and permanently through the origin. In this form the system is known as an ovonic memory switch; whereas the current below threshold is proportional to the contact area, the on-current is independent of it. This means that the on-state prevails not over the whole volume

of the device but only within a filament. Memory switches can be conveniently arranged into random access arrays ("read mostly memories") and are used for complex information storage. Such units are described by the endearing term "non-volatile" because the impressed information (that is, the existence of the on-state) does not depend on the continued presence of power supplies. Because memory as such is no virtue without a corresponding process of controlled forgetting, a reset procedure is also called for. This again takes the form of a current pulse (150 mA for 6 μs , say) but one with a sharp trailing edge and a higher rate of energy dissipation than the set pulse. The reset pulse therefore involves considerably higher filament temperatures, which are much greater than the liquidus temperature of the glass. The sharp trailing edge implies quenching, in the course of which the original off-state is restored. It is also known that filament formation is accompanied by crystallization processes.

In glasses which contain substantial amounts of Ge and Te, the filament consists chiefly of degenerate Te with a metallic-type conductivity; highly doped GeTe is a possible second phase among the Te crystallites. In the course of the reset pulse, the crystalline regions are redissolved and subsequently quenched back into the amorphous state. At Ann Arbor, Cohen, Neale and Paskin gave a detailed and convincing account of this process. Whereas the term "read mostly" is undoubtedly diplomatic parlance for "write rarely", the number of times a switch can be activated is not actually small. Individual units (as opposed to arrays) are now being routinely

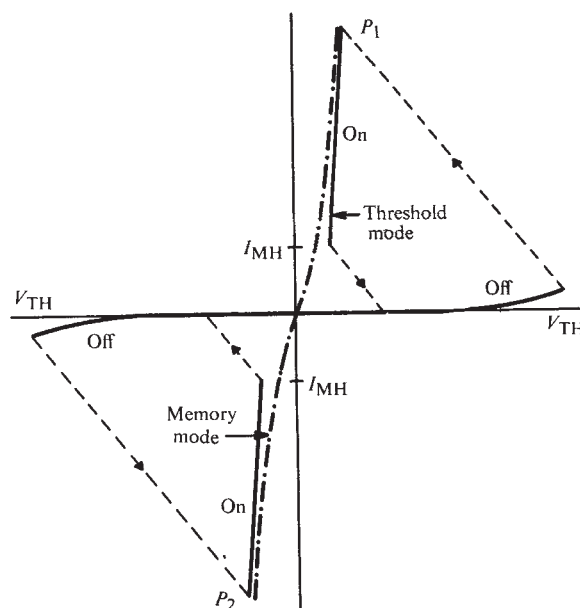


Fig. 1 Primary switching characteristics; threshold and memory models. Threshold voltage V_{TH} is approximately proportional to film thickness.

exercised with more than a million switching cycles, more than sufficient for applications, like micro-programming computer memories, machine instructions and telephone dial codes. The memories are interrogated (read) by much lower voltage signals and the number of read cycles is therefore almost unlimited.

The general principle of the memory switch is well understood but intriguing and important questions remain. How, for example, does the crystallization come about? Is it a homogeneous separation into two glassy phases originally present in submicroscopic form and does one of these phases later crystallize into the conductive path? (At the Ann Arbor conference opinions about this were divided. Roy *et al.* and Feltz *et al.* said yes; Moss *et al.* said no.) Alternatively, do the crystals form by nucleation within an originally single phase medium? If so, what is the nucleation mechanism and what, if anything, does it owe to the electrolytic (or at any rate polar) phenomena observed on some of the larger electrode systems? By now, it is strongly felt that these questions cannot be answered categorically for all systems, but must be examined separately for various families of alloys. There remains also the most important question of all: is the high temperature reached during the setting pulse a sufficient condition for the stabilization of the on-state or only a necessary one? The last question arises from the fact that memory switching always follows threshold switching. The stabilization occurs, therefore, when the system is in its (threshold) on-state and this makes it important to know the real nature of that state. The question is whether one is dealing simply with a hot filament, or with a state of electronic disequilibrium involving broken bonds, or (most probably) both. The mechanism of threshold switching is certainly a controversial point.

Filament Sizes

There is much evidence to suggest that typical on-state filaments have a cross-sectional area of the order of about $5 \times 10^{-8} \text{ cm}^2$. With on-currents of, say, 10 mA, this implies current densities of the order of $5 \times 10^5 \text{ A cm}^{-2}$ and in such conditions the notion of completely isothermal operation becomes implausible. Energy is being dissipated and because the medium is highly temperature sensitive (by virtue of its mobility gap) there are likely to be electrical consequences. The question, therefore, has never been whether heating effects are absent but whether their role is incidental (as in a transistor, for example) or necessary and sufficient (as in thermistor operation) or perhaps significant, in varying degree, but insufficient. In the context of the last possibility, it is immediately clear that the role of self-heating must increase with increasing film thickness. Because thermal and electronic processes can both lead to filament formation, such differences of mechanism may not show themselves at all clearly in the shape of the primary V - I switching characteristics.

Some heat development is inevitable and it was therefore natural and reasonable that attempts to explain ovonic threshold switching should concern themselves first with thermal models. Even though the concept of thermal breakdown is well established its detailed implications are only now beginning to be understood. Models which might be described as simple and purely thermal are those which contain $\sigma = \sigma_0 \exp(-\Delta E/kT)$, or some such term, as the only critical assumption. Such systems can certainly yield negative resistance behaviour (in the fashion of a thermistor) but, as is now known, never V - I relationships of the kind shown in Fig. 1, because it is a characteristic of threshold switches that the current cannot be stabilized in any way between the threshold points and points P_1 or P_2 (see conference papers by Kaplan and Adler and by Popescu and Croitoru). To achieve such characteristics on a thermal basis, it is necessary to postulate a lateral instability of the current distribution (that is, to envisage filament formation) arising from some secondary

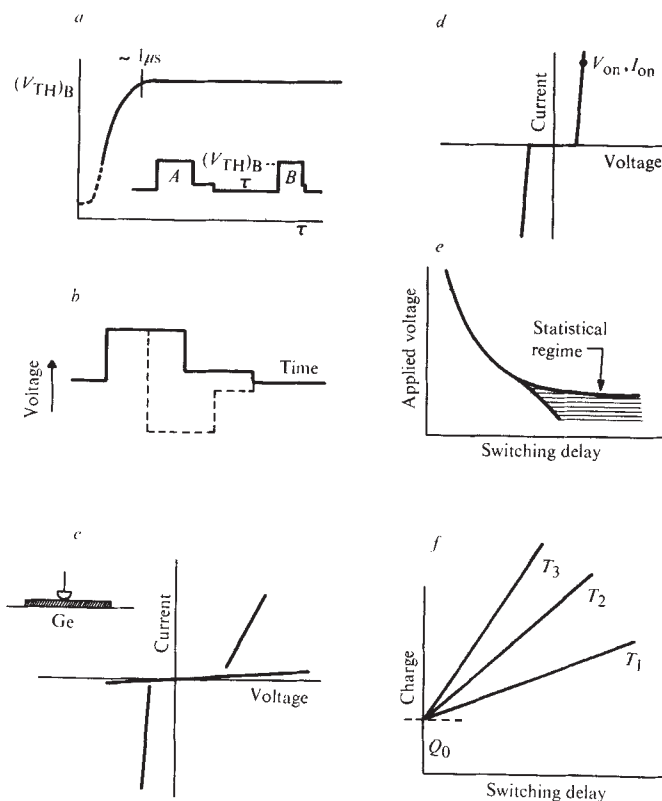


Fig. 2 Secondary threshold switching characteristics. *a*, $(V_{TH})_B$ independent of total energy dissipated by pulse *A* and, over a wide range, also independent of *A*-current in the on-state; *b*, lengthening of switching delay through pulse reversal, typical of various polar effects observed only at low temperatures; *c*, asymmetrical switching characteristics of a germanium-glass-graphite system (glass thickness $\approx 0.2 \mu\text{m}$); asymmetries reversed for n-type and p-type substrates (Henisch, Pryor and Vendura); *d*, transient on-characteristic, as determined by means of temporary ($\sim 0.1 \mu\text{s}$) excursions from the point V_{ON} , I_{ON} , (Henisch, Pryor and Vendura); *e*, statistical aspects of switching (Lee, Henisch and Burgess); *f*, Q_0 proportional to film thickness (Haberland and Stiegler).

cause. It does not matter, in principle, whether the filament is provoked by a thermal or an electronic fluctuation; its formation redistributes the current and thereby leads to switching. To achieve reasonable agreement on points of detail (like the shape of the on-characteristic and scaling of threshold voltage with film thickness) at least one additional assumption has, however, to be made: that the electrical conductivity of the medium is field dependent. On this basis, a remarkable degree of success has been achieved (Cohen and Kroll, Popescu and Croitoru, and Robertson and Owen, for example) in explaining the primary switching characteristics (Fig. 1). These models differ on points of detail but should always be called electro-thermal to express and maintain the crucial distinction from simple thermistor action.

Does a field dependent conductivity correspond to established facts? A field dependent conductivity $\sigma(F)$ is a plausible assumption pending direct experimental verification in the materials concerned. The corresponding experiments are not easy because electrode effects which could simulate a $\sigma(F)$ must be rigorously eliminated and because isothermal conditions must be assured despite the presence of high fields. If $\sigma(F)$ could be shown to be a reality, it might arise from one of two causes (or both): from a field dependent mobility or from a field dependent carrier concentration (by way of Poole-Frenkel). The last of these cases concerns, of course, an electronic disequilibrium situation and would at once involve us in questions of lifetime, trapping and space charge. Moreover it is principally through $\sigma(F)$ that electro-thermal models envisage switching to be related to the basic bulk properties of

the material concerned. Because of the key position which the $\sigma(F)$ assumption holds in electrothermal switching theories, its experimental exploration has become one of the most important pending tasks.

What are the features which the present electrothermal models cannot (yet) explain? Most of these come under the heading of secondary characteristics. Fig. 2 gives a digest, schematic and incomplete but broadly representative of the situation. To these results one must add some highly significant observations by Regel and co-workers on high temperature (500° to 600° C) switching in liquid semiconductors of widely varying conductivity.

How can such models be further developed and refined? The present electrothermal models neglect all contact effects (arising from barriers, injection and so on), all space charges (including those implied by the calculated non-linear field distribution) and their transport during switching, all possibilities of electronic disequilibrium in bulk (whether arising from impact ionization or the Poole-Frenkel effect or any other effect responsible for $\sigma(F)$), all trapping phenomena (including any relationship between switching and trap distribution which may exist in these materials). There is, therefore, both need (see above) and opportunity for further refinement, all of which will tend to emphasize the electrical aspects of the electrothermal models.

Are there alternative approaches which the available facts allow? Past attempts at interpretation began with purely thermal concepts and proceeded by introducing electrical terms when needed. (Thus Robertson and Owen refer to "electronically assisted thermal breakdown".) Because switching as such can in principle be obtained by purely electrical means, as

theoretically analysed by Mott, van Roosbroeck, Lucas and others, for example (pre-conference work), and also observed in various crystalline semiconductor systems, the opposite approach is also feasible, namely to begin with electrical concepts and to proceed by introducing thermal correction terms. Because of the complicated band relationship involved, most, though certainly not all, such attempts have in the past been only qualitative but there is every reason to believe that the situation can and will change. The question of which is the more important of the electrical and the thermal contributions may well turn out to have no precise meaning. It is already judged to be less important than it once was, partly because the calculated filament temperatures have been steadily decreasing (Cohen and Kroll) and partly because it is now known that threshold switches can withstand an astronomical number of switching cycles without sign of damage. On the other hand, every time the threshold switch is judged to be cooler than previously believed, the problem of interpreting the memory switch in purely thermal terms becomes increasingly severe.

The understanding of threshold switching has certainly not reached a stage which would permit the phenomenon to be used as a tool for the direct exploration of the amorphous state. On the other hand, this very possibility has been on the horizon since the non-thermal aspects of switching began to be recognized and it remains a reasonable hope that switching research will do for amorphous semiconductors what transistor research did for the crystalline variety.

¹ *Proc. Fourth International Conference on Amorphous and Liquid Semiconductors* (Ann Arbor, Michigan, August 9 to 13, 1971) (to be published in *J. Non-crystalline Solids*).

Three Dimensional Reconstruction from Serial Sections

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This article describes a technique for studying the detailed morphology of the central nervous system of a simple animal.

In the past ten years overwhelming evidence has indicated that in several vertebrates and invertebrates certain nerve connexions are established with an extraordinary degree of specificity, to the extent that functional connexions between repeatedly identified cells can be found in different animals of the same species¹⁻³. Somewhat more surprising is that, in animals which are capable of regeneration, contacts between identified cells can be reformed after lesion⁴ even

if the regenerating fibres are forced to travel through nervous regions completely unnatural to them⁵. Whether such specificity arises from different trophic substances mediating each contact or is simply a response on the part of the growing fibre to an overall biochemical milieu remains unknown.

In an attempt to elucidate the degree of specificity attained and to determine in what ways it may be altered, we studied the detailed morphology of the central nervous systems of two simple animals, the rotifer *Asplanchna brightwelli* and the crustacean *Daphnia magna*. These animals were chosen because each reproduces by diploid parthenogenesis, which makes it possible to obtain genetically identical clones; embryonic development can be also followed with some ease and each makes a clear behavioural response to light. In addition, the regions of neuropil mediating the response are sufficiently small that a whole cross-sectional area of the ganglion can fit into one field of view of a low magnification electron micrograph with no loss of resolution. This article describes our procedure for handling the large number of

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micrographs involved in creating a three dimensional reconstruction of the ganglion, the way in which information is recorded from them using a computer graphics terminal and how the data collected enable an unambiguous computer comparison of nerve cell topologies to be made. Detailed morphological results will be presented elsewhere.

Organization of the Micrographs

The reconstruction and visualization of three dimensional structures from micrographs of serial sections have long been important technical problems for biologists. This is true whether the micrographs are prepared with the light or electron microscope and whether one is trying to extract

useful information from sections of cell organelles, cells, organs or even whole organisms.

In the studies with the rotifer and daphnia we endeavoured to record the positions and shapes of cell bodies and of nerve fibres as well as synaptic contacts. These contacts are made entirely between the fibres in the neuropil, a region central to the cell body layer in invertebrate ganglia. These fibres may be as small as a few tenths of a μm in diameter and are extensively intertwined. For the rotifer, the region of interest is contained in a volume of approximately $100 \times 50 \times 40 \mu\text{m}^3$. Between 350 and 400 sections about 1000 Å thick were cut and photographed on 70 mm film with the Zeiss EM9S electron microscope at a magnification of $\times 650$. In the case of the daphnia eye-optic centre complex, about 2,000 sections of the same thickness were cut and photographed at a magnification of $\times 500$. With heavily stained material it is often useful to prepare sections for light microscopy which are as thin as 1 μm . Thus a large number of micrographs are necessary whether one is trying to reconstruct structures from electron micrographs of the nervous system of the small invertebrate or trying to visualize the three dimensional relationships of cells in developing embryo using optical microscopy. With current techniques of embedding, cutting, staining and preparing of micrographs, however, the difficulty in obtaining three dimensional information does not lie primarily in the preparation of the photographs of many serial sections but rather in making use of the photographs in such a way that useful information can be obtained.

In previous efforts the reconstruction has usually involved the preparation of physical models or artists' drawings of the structures under study or of outlines of them drawn onto transparent plastic sheets. Guideposts, either natural or artificially introduced during embedding, are used to align the traced images of the micrographs with respect to one another into a stack, which then becomes the desired reconstruction. There are certain difficulties inherent in these techniques which become more apparent when attempts are made to apply them to electron micrographs of regions of non-specifically stained neuropil where nothing is known about the fibres which are to be traced. First, useful models cannot be made thicker than a few fibre diameters, significantly less than the thickness of a ganglion. Second, it is impossible to include larger volumes by using partial reconstructions without already knowing a great deal about the pathways of the fibres to be followed. Third, it is difficult to obtain quantitative measurements from what is basically an object embedded in impenetrable plastic.

We therefore decided to adopt an alternative approach and first align the micrographs themselves with respect to one another and photograph them in their aligned positions, one frame per micrograph, onto successive frames of 35 mm film in order to make a ciné film through the region of interest. The abstraction process therefore takes place at the aligned stage, at which the micrographs can be scanned in a rapid, orderly manner, rather than at the unaligned stage at which they can be scanned *in toto* only slowly.

The machine used for this alignment and photography is shown, along with a schematic representation of the image combining principle used, in Fig. 1. It is well known that a comparison of nearly identical objects is most easily made by viewing them alternately at a rapid rate so we chose to use stroboscopic rather than incandescent illumination for viewing the micrographs. By controlling the frequency of flashes an operator can either see two items "simultaneously" (beyond human fusion frequency) or separately in rapid succession (below fusion). We have found the former mode convenient for rough alignment of transparencies but the latter, with its strongly induced illusion of motion between the nearly aligned pair, is indispensable for fine alignment. The operations involved in making the ciné film are straightforward and consist of photographing a transparency,

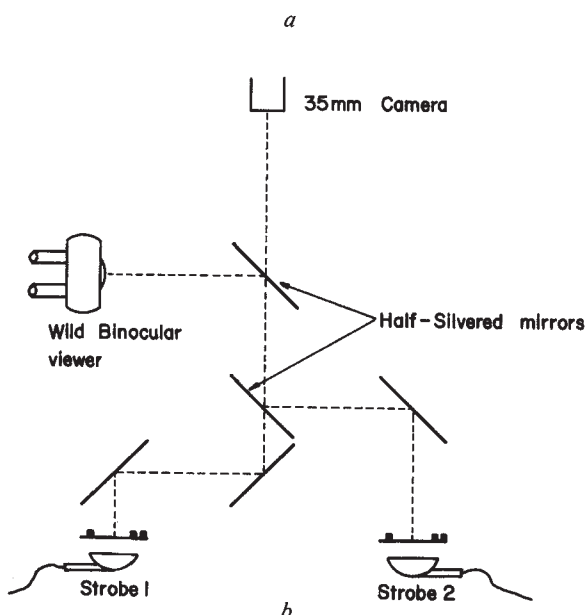
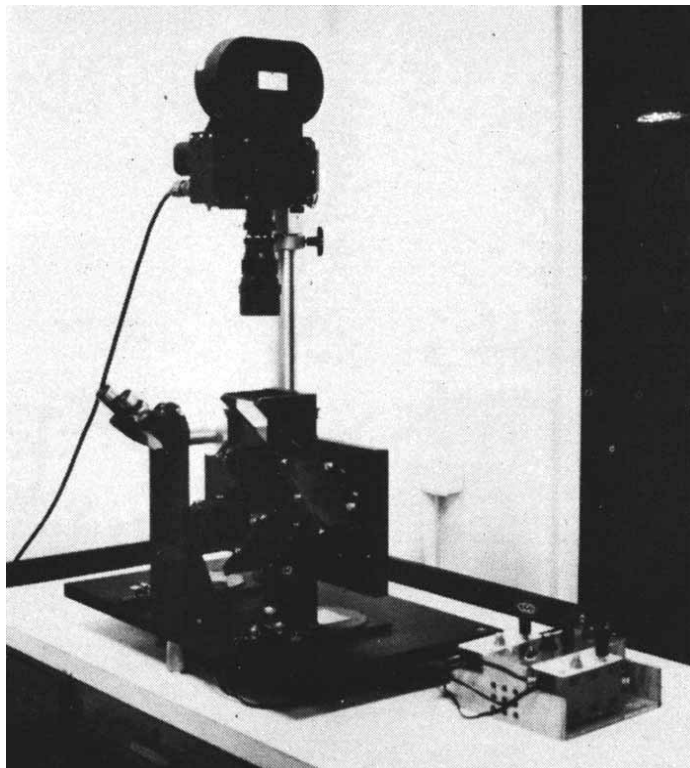


Fig. 1 *a*, Photograph of the ciné film making machine with 35 mm camera attached above. Strobe control box is at lower right. *b*, Schematic of the mirror arrangement used to enable simultaneous viewing of micrographs of sequential sections.

Fig. 2 Stereo pair of a contour drawing of the two anastomosing motor cells in the brain of the rotifer *Asplanchna brightwellii*. Dotted instead of solid lines are used. Spheres are random cell nuclei included to give a feeling for the extent of the ganglion and the placement of the motor cells within it. Photographs were made directly from the display screen of the Adage graphics terminal.



aligning the next one in sequence and then photographing it. This process continues through all the sections. In this way films can be produced for any material which can be sectioned, and the procedure is currently being used in our laboratory for reconstructing cell cleavage patterns during embryogenesis and following organelles of eukaryotic cells in addition to the neuro-anatomy referred to in this article. When a film made in this way is projected at normal motion picture speed, the observer has the feeling of "walking through" the material. He sees three dimensional relationships as the film is viewed.

Use of the Computer

Conceptually and operationally the use of the computer is divided into two parts which are treated independently: the collection of data about the pathways of individual nerve cells and the linkage of the cells into nerve aggregations. A researcher delineates the cells and their fibres using the computer as a notebook for recording three dimensional information, and the computer later uses the information given about the many individual cells at various points along their fibres to analyse the topological structure of the cells and the connectivity of the nerve network. This is fundamental, for we have found that a person without extensive training is easily able to follow a fibre through a series of aligned micrographs and make decisions as to branching and synapses, whereas teaching a machine to do this would involve extensive programming for pattern recognition. Because the recording of pathways, branches, and synapses requires only one passage through each fibre being recorded, it seemed that, at least for simple systems, people would turn out to be more efficient than machines. The chief data processing use of the computer is thus not in the interpretation of micrographs, but in carrying out the many-pass operations involved in linking together the individual neurones forming the network by using the synapse information supplied by the operator during the recording of the individual cells.

The facility used for recording structural information from the film is a computer with a graphical output operating with an interactive program which, as well as being able to record information on command, can cause the display of pertinent data already collected. These data are viewed with a device that superimposes the image of the film with that of a computer-driven oscilloscope. The recording of data is accomplished by two pieces of peripheral equipment, the first of which is used to specify the coordinates on the photograph. This is done by means of a computer generated spot on the oscilloscope screen whose coordinates are determined by the voltage drop across two potentiometers. These potentiometers are the two wheels, with perpendicular axes, of a small hand-held device (the "mouse"). The spot is moved to a position on the simultaneously viewed oscilloscope screen and film frame by rolling the mouse over a flat surface, and so requires no more mental effort to position than a pencil. This specifies the x and y coordinates of the point indicated by the operator. The computer is being used to control the projector and so it also has information about the frame number of the film, which in turn measures the z coordinate.

The second piece of peripheral equipment used is a set of

push-button switches. These control the computer program in such a way as to perform several tasks such as advancing the projector, recording the coordinates of the spot as part of the fibre, specifying it as a branch point, associating with the previously recorded point any one of a number of encoded properties (such as fibre diameter and synapse information) or handling the various file control options of the magnetic disk which is used for bulk storage of recorded structures. A fibre is "followed" in this way throughout the film using the computer to create a "nerve file" of co-ordinates. Such a file may also contain "tree" data when single lines are used to record only the position of the centres of fibres and their various branches. In either case, the coordinate information recorded in one or more nerve files may be displayed as a rotating projection in such a way that an observer sees the stored structures as three dimensional objects.

In recording nerve files, contour information is used in cases where one is particularly concerned with the external shape of the cell surface. For most fibre tracings, however, it is sufficient to use the line tracing, which preserves all the topological relationships and as many data of fibre geometry as the operator desires. The line description is a simplification which has the advantages that the amount of information which must be stored for what we consider a "complete" description is greatly decreased by comparison with carefully drawn contours or a completely digitized picture; it also lends itself to convenient mathematical abstraction. In a line structure, the nerve cell is regarded as a stick figure with the detailed pathways of its fibres reduced to an ordered

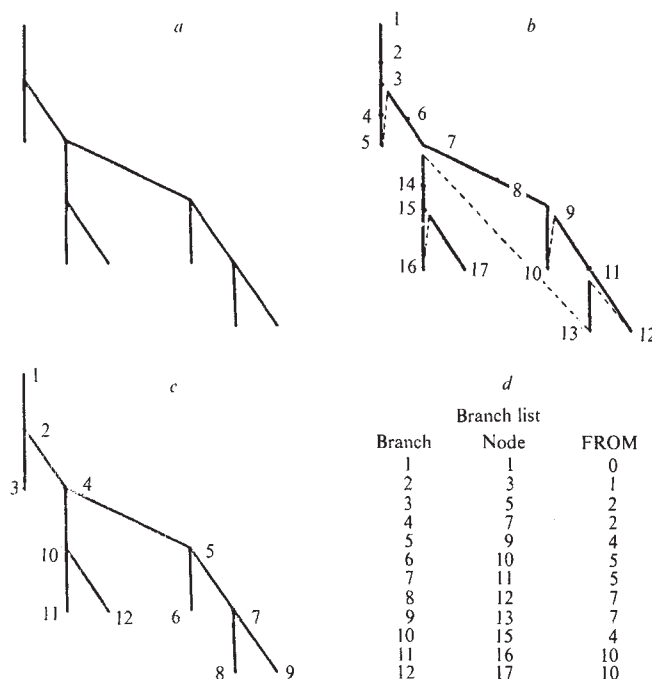


Fig. 3 Illustration of the principle used in tracing a branched structure. *a*, A tree; *b*, a possible tracing sequence. ---, Return from a terminus to the most recently recorded unsatisfied branch point; *c*, numbering of branch points only; *d*, topological specification of the tree.

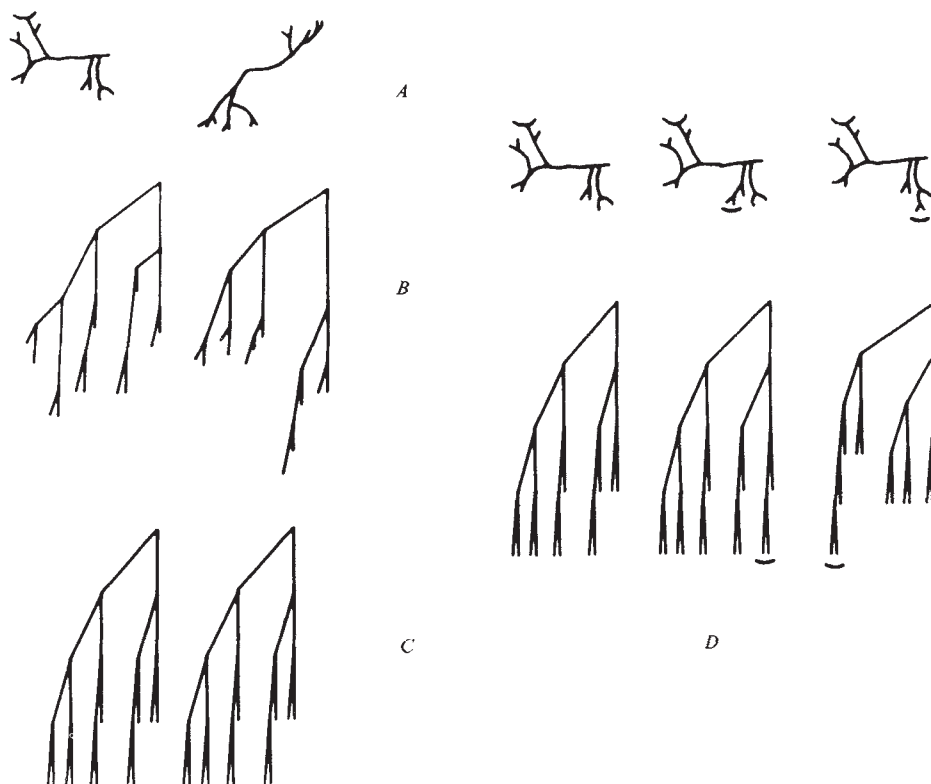


Fig. 4 Illustration of the formation of topological maps. The cells of *A* have been converted into maps in *B* and *C*. The topologies are the same; only the topographies have been changed to detect the coincidence. In *C* all lengths are arbitrary. In *B* the same manipulation has been done and the *x* distances are arbitrary, but the *y* distances are the contour lengths which, in the original structures, separate the branch points. The second type of conversion can be carried out in a straightforward manner by means of the corresponding FROM list only, whereas the first requires all the three dimensional information available about the paths between the nodes. In *D* one of the trees has been slightly altered to demonstrate the effect on the graph.

sequence of discrete points. To complete the description, there are one or more data associated with each point which give information about the fibre at that point in space.

The storage and use of data are best understood in terms of the graph theoretical concept of a directed tree. We consider nerve cells to be such trees, each point or node of which is classified as one of four types: a root (cell body), a terminus (end of a fibre), a branch point or a continuation (intermediate) point. At any desired interval Δz (which is taken to be an integral multiple of the section thickness) a point along the fibre is classified as one of the four types of nodes, numbered in sequence and then assigned coordinates and any other properties of a set the operator may choose to associate with it. Nodes which are branch points are placed at the top of a special list as they are recorded so that, when a terminus is reached, the computer is able to return the projector to the frame on which the most recently uncompleted node was recorded and display that node together with those branches which have already been recorded. The operator can see immediately where the remaining branches must be traced. A stereo pair of two fibres made by tracing in this way from micrographs of the almost bilaterally symmetric rotifer brain is shown in Fig. 2.

Topological Representation

Two types of numbering are carried out simultaneously and independently: (i) node numbering (of all nodes sequentially) and (ii) branch numbering (sequential numbering only of those nodes which are termini or branch points). The first is the means by which all nodes are catalogued and is used in the graphic representation of the nerve cell. The second is used in the description of the cell as a topological entity which is independent of its spatial characteristics. This is done by associating with each terminus or branch point, the branch number of the branch point from which it immediately comes, as well as its node number and any other properties. This association, the FROM list⁶, provides a direction to the edges of the tree and contains all the

topological information about the nerve cell. A simplified example of a tracing and numbering is shown in Fig. 3.

Several topological operations are useful in the manipulation and examination of nerve cell lists and can be carried out on the entire data structure by using only the FROM list. First, two lists can be added to join two structures which were traced separately; second, a list can be split into two lists, say, for the purpose of examining a part of a structure; third, the FROM list can be used for the creation of a two dimensional "stretched-out" representation of the tree described by the list. Thus a topological map of a nerve tree can be systematically prepared so that corresponding cells in different animals, or similar cells within the same animal, can be compared with varying amounts of three dimensional information suppressed. The construction of some topological map is shown in Fig. 4.

The data structure involved has obviously been made simple but with the possibility of expansion to arbitrary degrees of detail as long as this detail can be expressed in tabular form. It has been designed to record, in machine manageable ways, the topology, topography and abstracted detail of structures which are traced. The key figure, of course, is still the operator, who must interpret the micrographs himself; we have not created a completely automated analysis. Nonetheless this system has served to reduce the complexity of small regions of neuropil to allow a start to be made on the computerized study of the morphological connectivity of nerve integration.

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Ribosome Assembly in Hela Cells

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The 80S nucleolar particles have been found to contain peptides characteristic of 30S as well as 50S ribosomal subunits. This lends support to the idea that the maturation of both types of subunits stems from this 80S particle.

45S and 32S ribosomal precursor RNA can be extracted from Hela or L cell nucleoli in the form of 80S and 55S ribonucleoprotein particles, respectively¹⁻⁴. These particles are believed to be nascent ribosomes. The 55S particles appear by kinetic criteria and by polyacrylamide gel electrophoresis of their proteins to be direct precursors of cytoplasmic 50S ribosomes*, one or a few proteins apparently being added to the latter after their appearance in the cytoplasm^{1,5}. (The ribosomal proteins are synthesized on cytoplasmic polyribosomes⁶, thereafter migrating rapidly into the nucleolus for ribosome assembly.)

The position of the 80S nucleolar particle in ribosome assembly is less clear. An interesting possibility is that both 50S and 30S assembly commence together on 80S nucleolar particles at the level of 45S RNA. Polyacrylamide gel electrophoresis of mammalian ribosomal proteins has so far yielded insufficient resolution between 50S and 30S proteins to permit an examination of this question. Indeed, one does not know the extent to which mammalian 30S ribosomal proteins differ structurally from 50S proteins of similar electrophoretic mobilities (refs. 7, 8, and unpublished observations of B. E. H. M.).

An alternative procedure for comparing the proteins of the 55S nucleolar particle and the 50S ribosome should also be useful for further analysing details of the relationship between these two particles. Any alternative procedure should be suitable for use with small quantities of nucleolar material and applicable to kinetic experiments on ribosome formation. In the experiments to be described, Hela cells were labelled with ³⁵S-methionine, ribosomal subunits or nucleolar particles were prepared, their proteins digested with trypsin without further prior fractionation, and the digestion products "fingerprinted" on paper. This approach was based on a previous study of *E. coli* ribosomal proteins⁹. A brief summary of some of these results has been published¹⁰.

Methionine-containing Ribosomal Peptides

Fig. 1 shows autoradiographs of fingerprints of (a) 50S, (b) 30S and (c) an equimolar mixture of 50S and 30S ribosomal proteins from cells uniformly labelled with ³⁵S-methionine. Mixed subunits were used in Fig. 1c, rather than undissociated ribosomes, to avoid complications due to possible non-specific attachment of supernatant proteins to the latter. Considerable differences are evident between the 50S and 30S patterns, and several peptides which

are characteristic of one or other subunit are recognizable in the fingerprint of the equimolar mixture of 50S and 30S proteins. Eleven characteristic 30S peptides are shaded in the drawing in Fig. 1d. Six of these are normally fairly conspicuous in equimolar mixture digests, and are marked with arrows in the drawing. Three normally strongly labelled peptides which serve as useful "landmarks" towards the right of the fingerprints are marked black in Fig. 1d. Two of these (centre and lower right) are apparently common to both subunits, though in different relative amounts. Some ten to fifteen peptides (not specifically marked in the drawing) can be distinguished as unique to the 50S subunit. In some regions of Fig. 1c (for example, the top right hand section) it is not possible to distinguish peptides as being unique for one or other subunit, but the overall appearance of the peptide maps of the two subunits differs considerably even in these regions.

Similar experiments to those shown gave the following additional results. (i) Ribosomal proteins from subunits dissociated by high salt concentration¹⁴ yielded fairly similar fingerprints to those shown here, but there was evidence of some cross contamination of 50S with 30S material, due presumably to incomplete dissociation. (ii) ³⁵S-cysteine-labelled subunits yielded fingerprints which were different both from each other and from methionine-labelled subunits. There appeared to be no significant metabolic conversion of methionine to cysteine in our labelling conditions¹⁵. (iii) Fingerprints of proteins of ribosomal subunits from Hela monolayer cells were indistinguishable from those of *S. suspension* cells. All these results are consistent with the existence of major differences in primary structure between Hela cell 50S and 30S ribosomal proteins.

55S Nucleolar Particle

Our method should provide a sensitive independent check on the relationship between the proteins of the 55S nucleolar particle and the 50S ribosome. This relationship was examined by "pulse-chase" experiments (Fig. 2).

Fig. 2a shows a fingerprint of proteins from 55S nucleolar particles from cells which were pulse labelled for 30 min with ³⁵S-methionine. The pattern is similar to that shown for 50S ribosomes in Fig. 1a, except for somewhat shorter separation in the second dimension. However, the 50S ribosomal pattern after a 30 min pulse was quite different from that obtained in uniform labelling conditions. Most 50S ribosomal peptides were not significantly labelled, but a few peptides were prominently labelled. (There was also some streaking, which varied between preparations for pulse labelled material, and was probably due to contaminating cytoplasmic proteins, which attain high specific activity early in pulse labelling conditions.) After a chase with excess unlabelled methionine, the labelled peptides had largely disappeared from nucleolar 55S particles to appear on cytoplasmic 50S ribosomes (Fig. 2d), which now displayed a pattern resembling Figs. 2a and b superimposed. There was still faint residual labelling of some ribosomal peptides on nucleolar 55S particles after the chase, but no peptides had remained strongly or selectively labelled in the nucleolar compartment. This indicates that all the peptides seen in Fig. 2a are in fact on the pathway to ribosome maturation. (There is evidence that nucleolar particles also contain some protein of non-ribosomal type^{3,4}, possibly associated with the non-ribosomal regions of the precursor RNA molecules.

* The method used for preparing ribosomal subunits involved exposure of ribosomes to EDTA (see Fig. 1 and also ref. 5). Subunits prepared by this method sediment at 50S and 30S, respectively. Nucleolar particles, also prepared in EDTA buffer¹, sediment at 55S and 80S. The large and small ribosomal subunits are therefore designated 50S and 30S in this paper, although it is recognized that native or high salt derived mammalian subunits sediment at 60S and 40S, respectively.

This material becomes labelled much more slowly than ribosomal proteins on the particles⁴, and is evidently not revealed in pulse labelling experiments.)

By analogy with previous findings⁵ it seemed likely that some of the labelled peptides on pulse labelled 50S ribosomes (Fig. 2*b*) might be derived from protein which had specifically attached to pre-existing ribosomes before transfer of the bulk of newly synthesized material from the nucleolus had occurred. To examine this possibility cells were labelled with ³⁵S-methionine after preincubation with actinomycin D or toyocamycin, two substances which bring about almost complete arrest of maturation of new ribosomes from the nucleolus^{16,17}. The results show that several of the peptides seen in Fig. 2*b* are also found on 50S ribosomes in cells treated with these drugs (Figs. 3*a* and *b*). These peptides are therefore derived from protein which attaches to, or exchanges between, pre-existing cytoplasmic ribosomes. Two other strongly labelled peptides at the right of Fig. 2*b* are only weakly labelled on ribosomes from actinomycin or toyocamycin-treated cells. They seem to result from early or residual transfer of material which is first assembled into ribosomal particles through the nucleolar pathway.

80S Nucleolar Particle

The site of assembly of the small ribosomal subunit in mammalian cells has not been definitely established, but indirect evidence suggests that this, like 50S assembly, probably takes place in the nucleolus^{18,19}. Small subunits, like large subunits, enter the cytoplasm as such, having first passed through the nucleoplasm in the form of apparently intact ribonucleoprotein particles. (The quantity of 30S precursor particles in the nucleoplasm is, however, extremely small¹⁹.) Since most of the 18S RNA in the nucleolus is contained within 45S ribosomal precursor RNA molecules, which in turn can be extracted in the form of 80S ribonucleoprotein particles, it seemed possible that both 50S and 30S assembly might commence on these particles at the level of 45S RNA.

Figs. 3*c* and *d* show methionine peptide maps of two separate 80S particle preparations. The sucrose gradient from which the preparation in Fig. 3*d* was taken is shown in Fig. 4. The two fingerprints reveal predominantly 55S-like patterns, with weak labelling of a few (three to five) characteristic 30S peptides. We have obtained similar results from several 80S preparations. The 50S (or 55S) pattern is

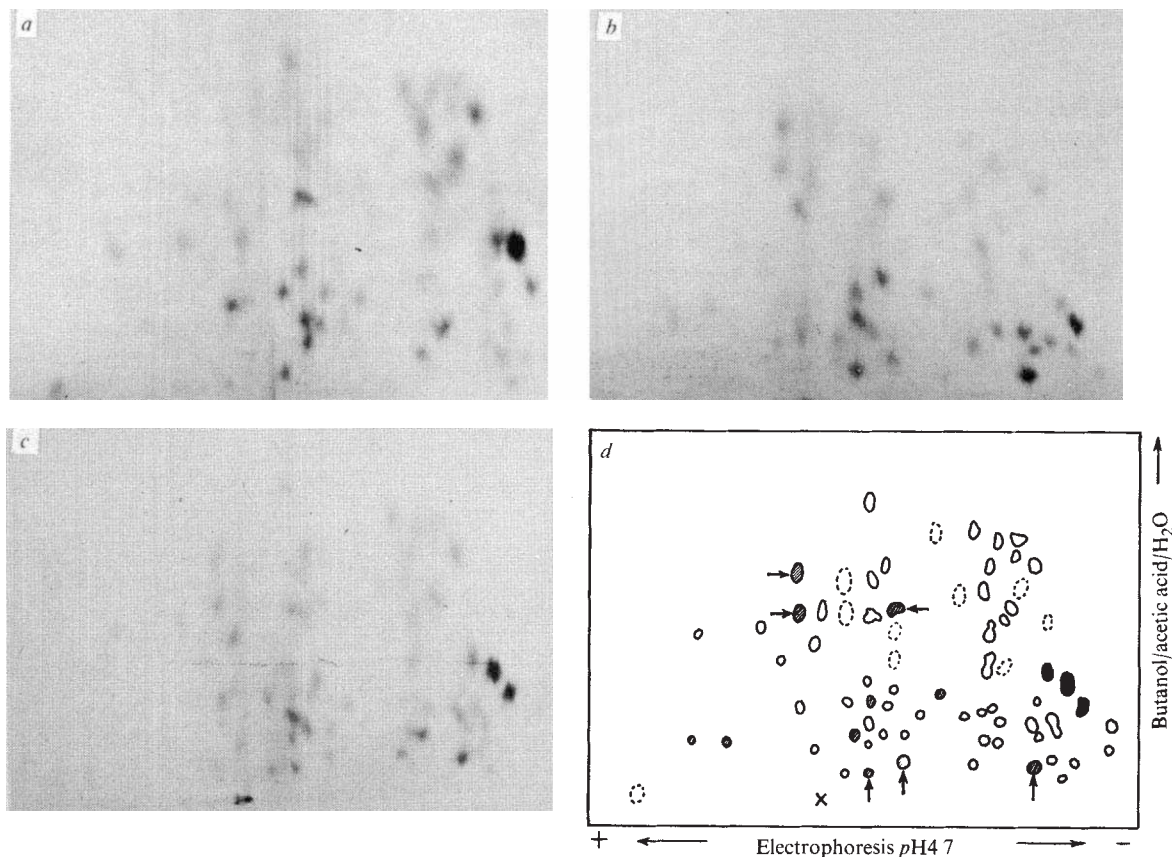


Fig. 1 Methionine peptide maps of HeLa cell ribosomal proteins. An initial inoculum of 2×10^7 HeLa cells was grown as monolayers for 72 h (three generations) in regular Eagle's medium¹¹ with 10% calf serum and 1 mCi ³⁵S-methionine (final specific activity 43.5 mCi/mmol). Ribosomes were prepared and dissociated into subunits as described by Warner⁵. The subunits were separated by centrifugation at 26,000 r.p.m. for 16 h at 0° C through 15–30% sucrose gradients containing NEB (0.01 M NaCl, 0.01 M EDTA, 0.01 M Tris HCl, pH 7.4) using the large bucket of the Spinco SW 27 rotor. The pooled peak fractions were dialysed for 18 h at 20° C against a large excess of distilled water, with 25 µg/ml. RNAase A (Sigma, protease free) in the dialysis bags to digest the rRNA. The proteins were lyophilized, oxidized with performic acid¹², lyophilized twice more, and digested with trypsin (TPCK treated¹³) in the presence of NH_4HCO_3 , pH 8.5, for 6 h at 37° C, using a 1 : 40 enzyme to substrate ratio. The quantity of substrate (ribosomal or nucleolar; Figs. 1–3) was estimated from the A_{260} of the original pooled peak fractions and the known RNA to protein ratio of the particles. After three further lyophilizations to remove NH_4HCO_3 the peptides were separated on 'Whatman 3 MM' paper by electrophoresis (2 h, 2.5 kV, 1.5% pyridine acetate buffer in H_2O) followed by descending chromatography (16 h, butanol : acetic acid : water 12 : 3 : 5). Radioactive peptides were located by autoradiography using 'Kodirex' film. The digestion and separation conditions described were standardized after preliminary experiments using a variety of conditions. Ribosomal proteins separated by treatment of ribosomal subunits with 4 M urea and 2 M LiCl gave substantially similar fingerprints to those shown here. The ribonuclease method was generally used because of its convenience for preparing small quantities of nucleolar material. *a*, 50S proteins; *b*, 30S proteins; *c*, equimolar mixture of 50S and 30S proteins; *d*, drawing of *c*. The dotted circles in *d* represent faint peptides which are more clearly seen in dense autoradiographs.

always clearly recognizable, but only a few 30S peptides are recognizable, and these are only weakly labelled. In no case has an 80S fingerprint resembled that of an equimolar mixture of 50S and 30S proteins such as that shown in Fig. 1c. The results of a reconstruction experiment with cytoplasmic ribosomal proteins suggested that the 30S peptides which are recognizable in Figs. 3c and d are present to the extent of about one-third or less of the corresponding molar amounts of 50S material.

Implications

The experiments described here provide evidence on the following points. (i) The fingerprints of cytoplasmic ribosomes point to considerable differences in primary structure between proteins from the large and small ribosomal subunits in a mammalian cell line. This result, though perhaps not surprising, was not fully evident from previous results using gel electrophoretic methods of protein separation^{7,8}. (ii) The pulse-chase and inhibitor experiments provide results which are in good agreement with earlier findings on the mechanism of 50S ribosome assembly in HeLa cells^{1,5}. Together the findings clearly establish that the major part of 50S assembly is completed in the nucleolus on 55S particles. The particles are transferred to the cytoplasm after cleavage of their 32S to 28S RNA. A small amount of protein of unknown function is added to, or exchanges between, 50S ribosomes after their appearance in the cytoplasm. (iii) The 80S nucleolar particle contains most of the characteristic 50S peptides (all of those found on 55S particles) together

with small amounts of a few characteristic 30S peptides (up to five out of a possible ten or eleven, the others being either absent, unresolved, or present in amounts too small for detection).

Since their initial discovery the precise position of 80S nucleolar particles in the sequence of events leading to ribosome assembly has remained an interesting unsolved problem. The finding that these particles contain 50S peptides together with small amounts of 30S peptides suggests that assembly of both types of ribosomal subunit at least commences on these particles. However, the significance of the relatively weak labelling of 30S material is not obvious. It is possible that the finding reflects an artefact of the method of preparation of the particles. The 80S particles seem to be substantially pure on re-centrifugation, indicating that cross contamination with 55S material is not the cause of the observed patterns. Selective detachment of 30S proteins during centrifugation of the particles is another possibility which it is difficult to eliminate, although it is not clear why such an effect would be restricted to 30S proteins. Alternatively the fingerprints may represent the true physiological state of the particles. It has been inferred from studies in which cycloheximide was used to inhibit protein synthesis that intracellular pools of proteins for 30S ribosome assembly may be much smaller than those for 50S assembly^{3,20}. There is also evidence that the kinetics of cleavage of 45S to 32S RNA are closely coupled to the rate of cellular protein synthesis^{4,20,21}, including, presumably, ribosomal protein synthesis. It is conceivable that interaction of 30S proteins

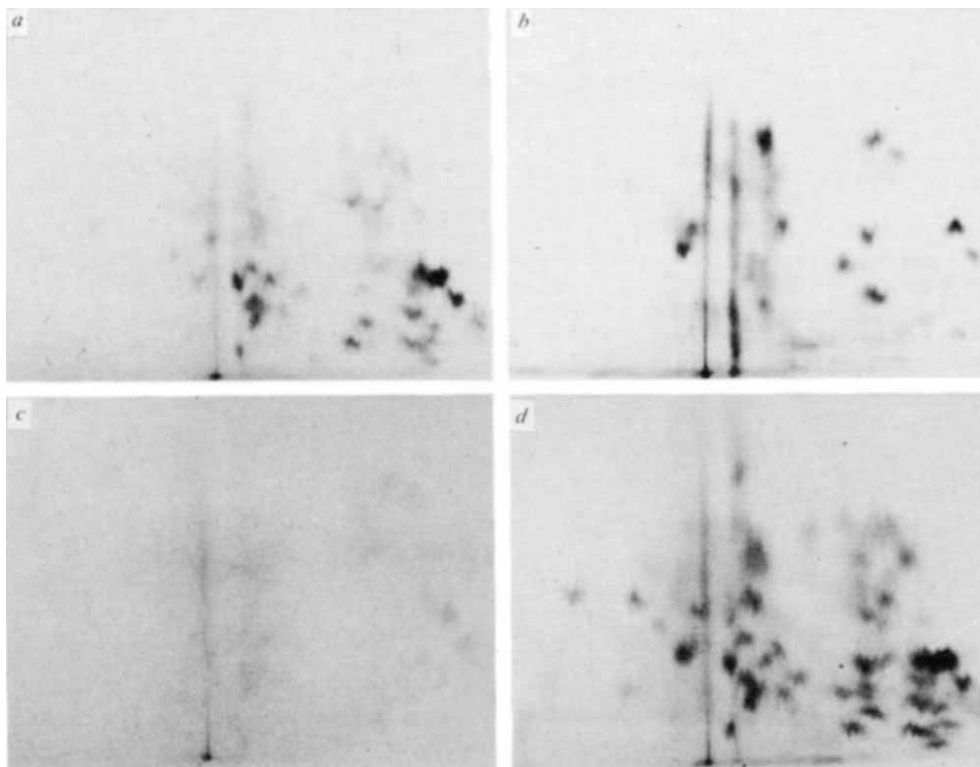


Fig. 2 Precursor-product relationship between proteins of nucleolar 55S particles and cytoplasmic 50S ribosomes. 3×10^8 S₃ HeLa cells were resuspended in 150 ml. of methionine-free Eagle's medium with 5% dialysed calf serum. 2 mCi of ³⁵S-methionine (18 Ci/mmol) was added, and one-third of the culture was collected after 30 min. Unlabelled methionine was then added to 0.5 mM and further aliquots of culture were taken at 30 and 180 min. Immediately after harvesting each culture, nucleolar particles were prepared by the method of Warner and Soeiro¹ and ribosomal subunits by the method of Warner⁵. In the preparation, a ball-type stainless steel Dounce homogenizer of 0.003 inch clearance was used for disrupting the cells in hypotonic buffer. A Dounce homogenizer of tighter clearance (0.002 inch), or a glass homogenizer with a 0.625 inch cylindrical plunger, both caused appreciable nuclear disruption, which resulted in partial degradation of nucleolar particles. Fingerprints were obtained as described in Fig. 1. *a*, Nucleolar 55S particles, 30 min pulse label; *b*, cytoplasmic 50S ribosomes, 30 min pulse; *c*, 55S particles, 180 min chase; *d*, 50S ribosomes, 180 min chase. All fingerprints are from the same experiment, except for *b* which was from a replicate experiment which gave a similar but technically better fingerprint. The 30 min chase samples are not shown; only a small amount of label had been transferred from 55S particles to 50S ribosomes at the end of this time.

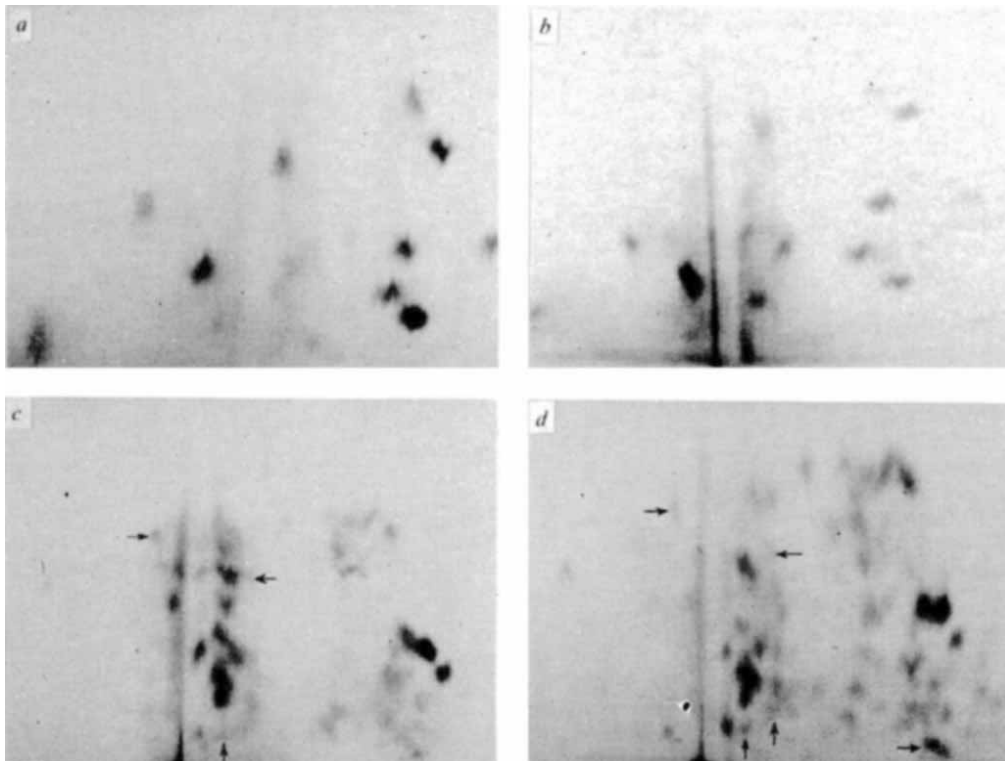


Fig. 3 *a* and *b*, Cytoplasmic exchangeable proteins on 50S ribosomal subunits. To two HeLa cell cultures, each containing approximately 1.5×10^8 cells, were added (*a*) actinomycin D, 4 $\mu\text{g}/\text{ml}$., and (*b*) toyocamycin, 0.2 $\mu\text{g}/\text{ml}$. After 1 h the medium was replaced by 50 ml. of methionine free medium with the respective inhibitors and 1 mCi of ^{35}S -methionine (17 Ci/mmol). After 1 h unlabelled methionine was added to 0.2 mM for 10 min to chase labelled nascent peptides off the ribosomes. The cells were then harvested, ribosomal subunits prepared, and the proteins fingerprinted as described in Fig. 1. The prints are slightly enlarged with respect to Fig. 2*b*. *c* and *d*, Methionine peptide maps of 80S nucleolar particles. *c*, Fingerprint of proteins from 80S particles obtained from the same preparation as the 55S particles in Fig. 2*a*. *d*, Fingerprint of another 80S particle preparation from 1.2×10^8 HeLa cells labelled for 30 min with 1 mCi of ^{35}S -methionine, 17 Ci/mmol.

with ribosomal precursor RNA is a limiting step in assembly of the 80S particle, and is immediately followed by cleavage of 45S RNA. A final possibility is that 30S assembly is completed after cleavage of the 18S sequence from 45S RNA, and conversion of the 80S particle into smaller products. No specific 30S precursor particle has been detected in nucleolar extracts although, as noted above, very small steady state levels of 30S particles occur in the nucleoplasm¹⁹. Further experiments along the lines described in this paper may clarify some of the remaining questions.

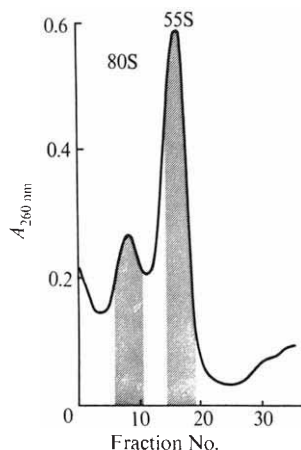


Fig. 4 A_{260} profile of nucleolar particle preparation used for obtaining the 80S fingerprint in Fig. 3*d*. The fractions taken for fingerprinting are indicated by shaded bands. (The 55S fingerprint is not shown here, but similar fractions were taken for the 55S preparations shown in Fig. 2.)

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New Zirconium-rich Minerals from Apollo 14 and 15 Lunar Rocks

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Two more members of the suggested Zr-Ti-Fe mineral group of lunar oxides have been discovered. They have similar optical and chemical properties to the two such compounds previously detected, but all four show considerable differences in their detailed chemistry.

A CHARACTERISTIC feature of lunar basalts is the presence of rare oxide minerals rich in zirconium, titanium and iron, associated with small patches of residual granitic glass. These minerals have not been found on Earth and are sufficiently variable in composition to warrant consideration as members of a Zr-Ti-Fe mineral group. One member has already been named¹ "tranquillityite" and another, of a different composition², has been called "phase β ". Each is characterized by fairly abundant yttrium and rare-earth elements, and phase β is unusually rich in niobium, lead, thorium and uranium.

We have discovered another two minerals of this group by electron-microprobe analysis. One ("phase X") is in a feldspar-phryic basalt from the Fra Mauro formation (14310) and the other ("phase Y") in a pyroxene-rich ferrobasalt from the rim of Hadley Rille (15555). They have the same general optical and chemical properties as tranquillityite and "phase β " but the four together show appreciable chemical differences in detail.

The literature on lunar mineralogy is becoming confused because of oblique references to various new phases by different investigators. Here we propose a basis for a nomenclature which can be applied to other group members that may be found as investigations proceed. We also emphasize the need for experimental synthesis of the Zr-Ti-Fe oxides in order to establish the degree of isomorphism displayed between members of the group.

In our nomenclature, the four phases are considered as members of a "tranquillityite group", characterized by fairly low amounts of CaO (<3% weight). There may be a more calcic group in the lunar rocks, referred to as "dysanaltyte"³ and "phase B"⁴. But no specific values for calcium have been given during reference to Ca, among other elements, as a "major" constituent³⁻⁵. Phase β and our phases X and Y all contain three times the amount of CaO found in tranquillityite (1%) but not to the extent of being a major constituent. Terrestrial dysanaltyte⁶ is a niobian perovskite which contains about 26% CaO and no detectable ZrO₂. At present we urge investigators not to refer to any lunar minerals as "dysanaltyte-type" until there are data on their calcium and zirconium contents. It has been suggested that phase B could be related to terrestrial zirkonolite⁴ but this is also a calcic mineral (CaZrTi₂O₇). We find that terrestrial zirkelite⁷ bears the closest comparison with the tranquillityite group, and yet contains sufficient CaO (10.8%) to provide a possible link

with any calcic lunar zirconian phases yet to be established and analysed.

New Lunar Minerals

The two new minerals are very similar in occurrence, crystalline habit and optical properties to tranquillityite. Both occur as rare, small crystals (12-40 μ m) in the residual mesostasis of lunar basalts. The mesostasis includes baddeleyite, whitlockite, K-Ba feldspar and rhyolitic glass, as well as the Fe-rich fringes of pyroxenes and olivines. In one case (14310), tranquillityite is common as 25 μ m grains, separate from phase X.

Both share with tranquillityite and phase β a dark, reddish-brown colour in transmitted light, being near-isotropic and of high refractive index. In reflected light, the grains are pale grey and either rectangular or sheaf-like in habit. Only one small crystal of each new phase was detected, so we cannot offer any views on their crystal structure (tranquillityite is hexagonal¹, and terrestrial zirkelite is either hexagonal or rhombohedral⁷).

The chemical compositions are given in Table 1, with comparisons. For convenience in cross-reference, tranquillityite is numbered according to its Apollo type-locality (11), and the other three phases according to the Apollo suite in which they were first discovered. The names "phase X" (14) and "phase Y" (15) are used in this text. Nos. 12, 14 and 15 differ from tranquillityite in having low SiO₂. Otherwise the greatest major variables are TiO₂, FeO and ZrO₂, which together account for most of each mineral composition, and which have led to the proposition here that variation within the group should be considered chiefly according to the system shown as Fig. 1.

The points on Fig. 1 show a wide spread in compositions, even if confined to the three major oxides. The total weight contributed by ZrO₂+TiO₂+FeO varies from 88% (14) to only 51% (12), but in the latter case the FeO content is variable from grain to grain² compared with the next most abundant oxide (Y₂O₃). There is a great deal of variation, among the phases, in regard to the elements next in abundance to Zr, Ti and Fe. The fourth and fifth in abundance are shown in parentheses for each phase (Fig. 1). The data in Table 1 show a complex variation between the phases, but the diagram illustrates the main variations. Other terrestrial-type minerals occur with these new phases in the lunar rocks and serve to emphasize the validity of the ZrO₂-TiO₂-FeO system in this context. Shown on Fig. 1 are baddeleyite (B), the ZrO₂ end-member containing hafnium¹⁰; rutile (R), the TiO₂ end-member which is sometimes niobium-bearing⁸; and ilmenite (FeTiO₃) which is sometimes zirconian ilmenite (ZI) in the lunar rocks⁹. Hence there is the basis here for predicting a more extensive display of the ZrO₂-TiO₂-FeO system in the lunar rocks than found in terrestrial rocks, including in particular the participation of Y, Nb and the rare-earth elements (REE). Zircon (ZrSiO₄) is rare in the lunar basalts, emphasizing that silicates of zirconium, common in terrestrial granites, are subordinate to silica-poor and silica-free zirconian phases in the residual lunar granitic glasses.

quillityite¹ have shown a range in composition according to the rock numbers. The phase is particularly common in a feldspar-phyric basalt (14310) and so we analysed six different grains to compare with our previous analysis of Apollo 12 tranquillityite¹⁰ and with the data from other investigators¹. The result (Table 2) when compared with the earlier mean values (Table 1, 11) shows a slight but significant increase in TiO₂ relative to ZrO₂, and a sharp fall in Y₂O₃. This is the case when compared, also, with our own analysis of Apollo 12 tranquillityite¹⁰.

The discovery of phase β by Haines *et al.*² was the first indication of strong variation in the composition of phases that could otherwise be referred to as Zr-Ti-Fe rich oxides. (Unfortunately, a typographical error in their Table 2 ("phase A") implied that tranquillityite was a very calcic non-silicate. Their quoted values for SiO₂ and CaO should be transposed.) The two additional new minerals described in the present article do not show the remarkably high niobium, lead, thorium and uranium contents exhibited by phase β . A search for comparable terrestrial minerals has, however, shown that terrestrial zirkelite⁷ is the closest analogue (Table 1, TZ). This is particularly so in regard to the high contents of ThO₂ and UO₂. The mineral occurs in the type example of jacupirangite (Brazil), with perovskite and baddeleyite. There is still some doubt⁷ as to its crystal system (hexagonal or rhombohedral) and also a modern chemical analysis is desirable in view of its calcic nature (Table 1) and hence a possibly close link with calcic-zirconian lunar phases referred to earlier in this paper.

Genetic Considerations

The discovery of lunar tranquillityite in late 1970 has been followed by the discovery in 1971 of at least three other members of this new mineral group. Although the crystals are small and rare, they are almost ubiquitous in the granitic residuum of the lunar basalts. We have suggested¹⁰ that the term "KREZP" (potassium, rare earths, zirconium and phosphorus) would be better than KREEP in drawing attention to the nature of this residual fraction, and this becomes even more important when the peculiar chemistry of the tranquillityite mineral group as a whole is considered (Table 1). The occurrence of tranquillityite in granophyre is a further reminder that concentrations of Zr, Hf, Y, REE, U or Th may be a good guide to the nature of the source rock containing minerals of this group, as well as using the concentrations of K, Ba and P.

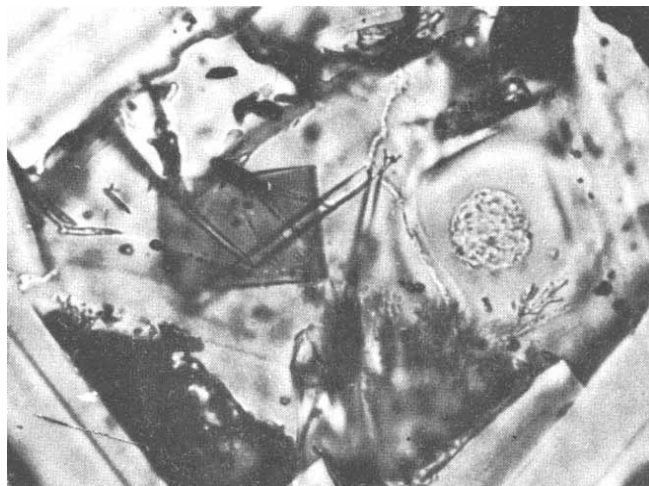


Fig. 2 Photomicrograph of tranquillityite, the dark-toned rectangle (16 × 32 μm). Occurs between plagioclase laths in the mesostasis of a lunar basalt (14310/20). See Table 2 for analysis. The other zirconian phases (Table 1) have similar size, habit and optical properties.

These elements, as detected by X-ray fluorescence analysis (carried out by J. G. Holland, Durham), are K, Rb, Ba, Y, Zr, La and Nb. They are the elements concentrated in the barian sanidine and tranquillityite-group minerals, and found to be associated with granophyre and rhyolite in the lunar rocks. The importance of anorthosite as a lunar crustal material has rightly been stressed, but this has led to neglect of the concept that granitic material (as in the Earth's crust) is probably an important component of the Moon's crust. The concentration of granitic material in the Fra Mauro soils (Apollo 14) is obscured because of the low melting temperature of this material, which is present chiefly as a component of hybrid glasses. Within this granitic material, probably produced from the fractionation of lunar basalt beneath a primitive anorthositic crust, resides a strong concentration of the heat-producing elements (K, U, Th). Thus calculations of the amounts of these elements in the lunar basalts would lead to a strong under-estimate of the contents in the whole Moon.

Our co-investigators at Durham, Dr C. H. Emeleus and Dr J. G. Holland, offered helpful advice. This research is supported by a grant from the Natural Environment Research Council.

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Table 2 Analyses of Six Crystals of Tranquillityite from Apollo 14 Feldspathic Basalt (14310/20)

	1	2	3	4	5	6	Mean
SiO ₂	13.78	14.19	13.62	14.09	16.19*	14.19	13.97
TiO ₂	23.19	22.16	20.77	21.31	21.53	22.64	21.93
Al ₂ O ₃	1.06	1.09	1.30	0.93	1.30	1.46	1.19
FeO	41.95	43.56	42.30	42.49	40.95	41.57	42.14
MnO	0.23	0.20	0.26	0.22	0.35	0.44	0.28
MgO	1.49	0.76	1.05	1.34	1.68	1.45	1.30
CaO	1.08	1.08	1.11	1.33	1.06	1.03	1.12
ZrO ₂	13.90	9.82*	15.41	14.62	14.97	13.76	14.53
Cr ₂ O ₃	0.11	0.35	0.14	0.14	0.20	0.23	0.21
Y ₂ O ₃	0.50	0.52	0.51	0.51	0.50	0.50	0.51
	97.29	93.73	96.47	96.98	98.73*	97.27	97.18

* These amounts seem aberrant, perhaps because of probe-spot wander into the matrix. The values have not been included in the mean.

A significant feature of the trace-element analyses of lunar regolith "soils" is the progressive increase in certain elements from Apollo 11 through Apollo 12 to Apollo 14 samples.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Nature of the Secondary Component of Beta Lyrae

AMONG known binary systems suggested¹⁻⁶ as possibly harbouring a black hole as a secondary, ϵ Aur⁷⁻¹¹ and β Lyr^{12,13} have drawn much current attention. Both systems consist of a luminous massive primary and a faint (or invisible) secondary, whose presence is revealed largely by the eclipses it produces. From the mass function alone, each secondary must be fairly massive and is probably in the form of a disk (or ring) containing an underluminous star. This latter star has been suggested as being a collapsar.

In the case of β Lyr at least, an alternative hypothesis regarding the nature of the secondary star seems possible. We suggest that it may be a massive "main-sequence" star in rapid, nonuniform rotation. Specifically, we are adopting Huang's¹⁴ and Woolf's¹⁵ basic model for β Lyr, consisting of a faint star embedded in a circulating disk that has formed as a result of the primary's overflowing its Roche lobe during evolutionary envelope expansion (except that, in our picture, the disk need not be massive). There are two other examples of stars whose underluminosity is probably due to high angular momentum. The importance of these two stars is that they are normal enough not to be accused of harbouring a black hole.

R. S. has recently prepared a catalogue containing data for seventeen main-sequence OB components of twelve massive binary systems, for which reliable masses and luminosities of both components are available; most of the luminosities are based on distance moduli of the clusters to which these selected systems belong. In a plot of mass against spectral type (or effective temperature), all but two of the components lie within the theoretical main-sequence band based on nonrotating stellar models (with a small allowance for uncertainty of the "normal" Population I chemical composition). A similar result is obtained in a plot of mass versus luminosity.

Table 1 Deficiency of the Luminosity and Effective Temperature of the Primaries of μ^1 Sco and V356 Sgr with Respect to Nonrotating Stellar Models

Primary	Sp	$M/M_\odot$	M_{bol}	$\log T_e$	$\delta[M_{\text{bol}}]$	$\delta \log T_e$
μ^1 Sco	B1.5 V	14	-4.5	4.33	~ 1.5	~ 0.10
V356 Sgr	B3 V	12	-3.6	4.25	~ 1.5	~ 0.10

The two exceptions, μ^1 Sco and V356 Sgr, have primaries that are very cool and underluminous for their masses, as is shown by Table 1. For V356 Sgr, the luminosity has been determined only from the effective temperature combined with the radius given by the orbit solution; but for μ^1 Sco, three independent methods have been used: first, effective temperature and radius from the orbit; second, photometric distance modulus from membership in Sco OB2; third, kinematic distance modulus based on membership in the Sco-Cen moving group. All three methods give virtually the same luminosity for μ^1 Sco. Harris, Strand and Worley¹⁶ classify the masses and radii from the orbits of μ^1 Sco and V356 Sgr as fairly reliable, while Wood¹⁷ designates them as "well determined".

One evolutionary feature differentiates the primaries of μ^1 Sco and V356 Sgr from all the other OB components under consideration (except Z Vul). They are almost certainly the former secondaries in systems that underwent a mass exchange, since the present subgiant secondaries have very low masses but are more highly evolved than the primaries¹⁸. L. B. L. has pointed out previously¹⁵ that, during the mass-exchange process, appreciable orbital angular momentum is expected to be picked up as rotational angular momentum by the (new) primary. Turbulent convection may, on theoretical grounds, be supposed to mix the star, chemically and rotationally, on a fast (Kelvin) time scale, tending to produce a "zero-age" main sequence star in approximately uniform rotation¹⁹. But viscous forces near the surface where the primary is still attached to the remnant of the massive disk, and tidal forces due to the presence of the companion, will tend to slow down the rotation of the stellar envelope whereas the denser core will be much less retarded. But even if the mixing does not extend to the centre and thus leaves the core rotating with its initial (small) angular momentum, the reduced central pressure, compared with that in a nonrotating star of the same mass in which the weight of the overlying layers is fully felt (since it is not reduced by centrifugal force), will produce the same effect of a lowering of the surface luminosity as does a reduced central pressure due to fast rotation in the core. Our point is that, regardless of the extent of internal mixing induced by the process of mass accretion, the primaries of μ^1 Sco and V356 Sgr are expected to be in rapid, highly differential rotation, compared with the probably uniform rotation of the other 15 stars in our sample. The known surface rotational velocity of the primary of μ^1 Sco, $V_e = 220$ km/s, is consistent with the values for the other stars. In fact, synchronism of the surface rotational period of the primary with the revolutional period seems to have been already attained in μ^1 Sco, though not in V356 Sgr²⁰.

It is well known that a uniform rotation imposed on stellar models has very little effect on the surface luminosity but reduces slightly the effective temperature (making the spectral type appear later)²¹. Recent models of Bodenheimer²² for massive main-sequence stars in highly nonuniform rotation show that both luminosity and effective temperature can be drastically reduced by concentrating angular momentum to the centre of the star, even for modest surface rotational velocities. A typical magnitude decrement due to differential rotation with $V_e = 300$ km/s is 1 mag, but it could be even larger according to Bodenheimer.

Uniform rotation with $V_e \approx 200$ km/s would not greatly change the effective temperature of a massive main-sequence star, thus probably accounting for the agreement between theoretical nonrotating stellar models and the 15 "normal" stars in our sample. Nonuniform rotation, however, seems the only way to explain the observed properties of the primaries of μ^1 Sco and V356 Sgr, and is in accord with evolutionary theories concerning these two systems. A possible check on our idea would be to show from an analysis of accurate light curves that the shapes of the primaries are inconsistent with their observed surface rotation and the hypothesis of uniform rotation. In the case of μ^1 Sco, the orbital inclination may be too small (60°), and the tidal

distortion too great²³, to make a reliable check. In the case of V356 Sgr, the orbital inclination is approximately 90° and the components are well separated. The difficulties encountered by Popper²⁰ in analysing the light curve of this system might lead one to suspect that the primary does indeed have an anomalous shape. It would be worthwhile for someone to reobserve and reanalyse these two systems in more detail, along the lines recently begun, for example, by Wilson and Devinney²⁴.

Returning to the problem of β Lyr, we suggest that, if the "secondary" has already accreted most of its massive disk, it may be in rapid, highly nonuniform rotation. It could easily be underluminous by 2 mag, or more, for its mass. (Devinney's observational estimate of the amount of underluminosity, 4 mag, is probably an upper limit, as may be judged from his published data¹²; a value of 2 mag seems more reasonable and has, in fact, been estimated by Woolf¹⁵.) The secondary would further be expected to exhibit all the emission characteristics of an extreme Be star, but these will, of course, be considerably modified by the presence of the remnant disk. Woolf²⁵ has pointed out that the secondary should be the less evolved component, on the basis of elementary considerations of evolution as outlined above, and he has also¹⁵ mentioned several analogies between this system and the somewhat more evolved system V356 Sgr. In contrast, Devinney's alternative theory of the origin of the disk¹², which is similar to that proposed⁸ for the disk in ϵ Aur, does not account for the peculiar properties of the primary, such as the filling of its Roche lobe and its hydrogen deficiency (compare the apparently normal primary in ϵ Aur whose separation from the secondary is probably too great for the components ever to have interacted significantly). These reasons make it hard to believe that a collapsar is embedded in the disk of β Lyr (unless a second phase of mass transfer has again interchanged the roles of primary and secondary—but time scale arguments militate against the probability of observing such systems). Accretion of matter from the remnant disk would still occur for the massive secondary, and may, then, still account for the "blue" spectral energy distribution that is observed^{13,26}.

We conclude that, before the inference of a collapsar in β Lyr and in similar systems (such as ν Sgr, KS Per, UW CMa, V353 Sco, and HD 47129) can be made plausible, the more likely explanation of differential rotation must be investigated more fully. In particular, it would be valuable to determine theoretically the maximum amount of underluminosity for a model of the secondary of β Lyr that is compatible with dynamical stability and with the requirement that the equatorial radius does not exceed the size of the Roche lobe.

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Did Southern Africa and North America Drift Independently during the Precambrian?

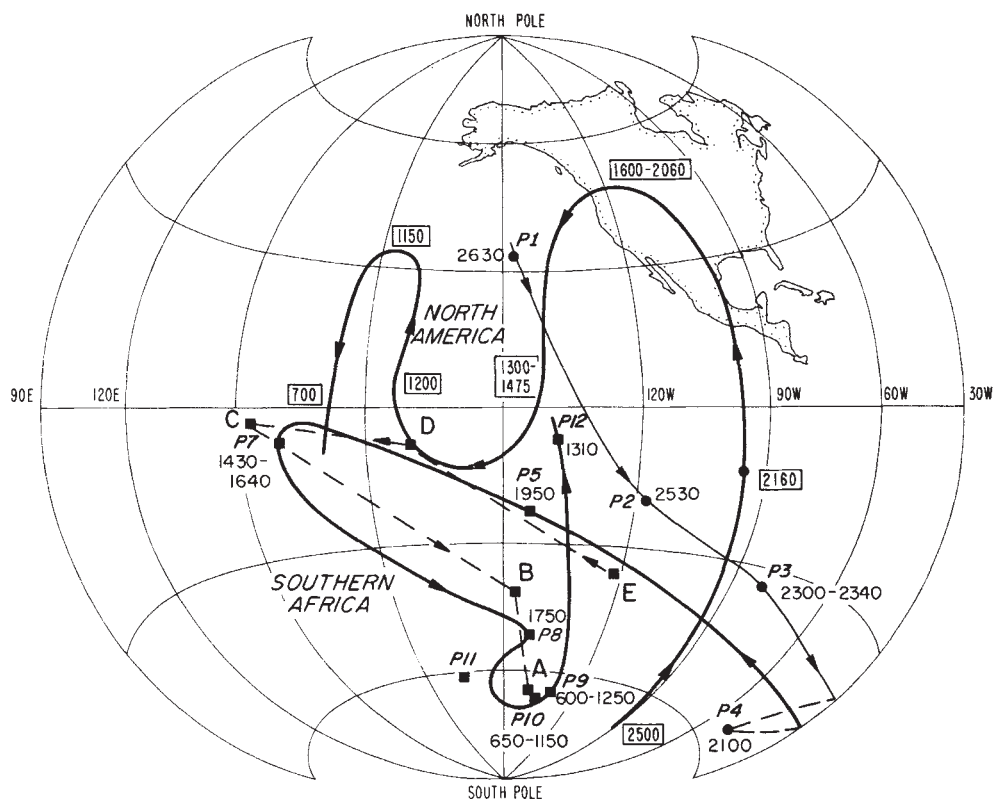
THE pattern of continental drift and seafloor spreading since the Jurassic is well established, and there is now some interest in investigating pre-Mesozoic drift^{1,2} using palaeomagnetism. Comparison of pole paths from different continental plates over the same intervals of geological time to see whether they can be superimposed indicates whether during these intervals the two plates were contiguous³. Because the Precambrian occupies over 80% of geological time, palaeomagnetism is important in deciding whether continental drift has been a catastrophic or a uniformitarian event in Earth history. This communication describes an attempt to reconcile the presently defined Precambrian pole paths for Southern Africa and North America in terms of the computer fit of the continents around the Atlantic¹⁶.

Palaeomagnetic studies of Precambrian rock units involve four important factors. First, the isotopic age may be resolvable only to 100 million years (m.y.)⁴. Second, the Precambrian record is nowhere complete: thus it may prove impossible either to show consistency in the pole path using rocks of the same age but from different locations, or even to construct a representative pole path for certain continents. Third, the present continents may not always have been single Precambrian cratons: they may have formed by welding of several plates⁵. Fourth, the magnetic stability and reliability of Precambrian rocks must be carefully established⁶.

McElhinny *et al.*⁷ constructed Precambrian pole paths for the Rhodesian and Transvaal shields of Southern Africa (Fig. 1). Some twenty determinations were used from separate rock units ranging in apparent age from 1,310 to 2,630 m.y. Although the poles were of high magnetic quality, the isotopic ages of some of these rock units were considered to be preliminary. In Fig. 1, note the apparent inconsistency between the isotopic and magnetic ages for P7, the 1,430–1,640 m.y. Mashonaland dolerites²⁰, and P8, the 1,750 m.y. Premier Mine Kimberlite²¹. Nevertheless the agreement between poles from diverse igneous rocks and the thick red bed sequence of the Waterberg Series²² provided a good consistency test for the pole path during the interval 1,310–1,950 m.y. Additional data for younger rocks from Tanzania do not simply fit into this pole path⁸ and may indicate that the Tanzania and Rhodesian/Transvaal cratons behaved as separate plates during the Precambrian. For the interval 2,100–2,630 m.y., two alternate paths were proposed⁷, because of the large distances of arc required to join poles from 1,950 and 2,100 m.y. rock units respectively.

Although palaeomagnetic studies have been made on rocks from Australia⁹ and the Baltic shield¹⁰, North America is the only other continent where sufficient numbers of dated Precambrian poles of different age allow a representative pole path

Fig. 1 Precambrian pole paths with isotopic ages in million years for Southern Africa (after ref. 7) and North America (ref. 6). The African poles, P1 to P12, with apparent ages are from Table 1 of ref. 7: the poles E to A linked by the dotted line are an upward stratigraphic sequence of the Waterberg Series²².

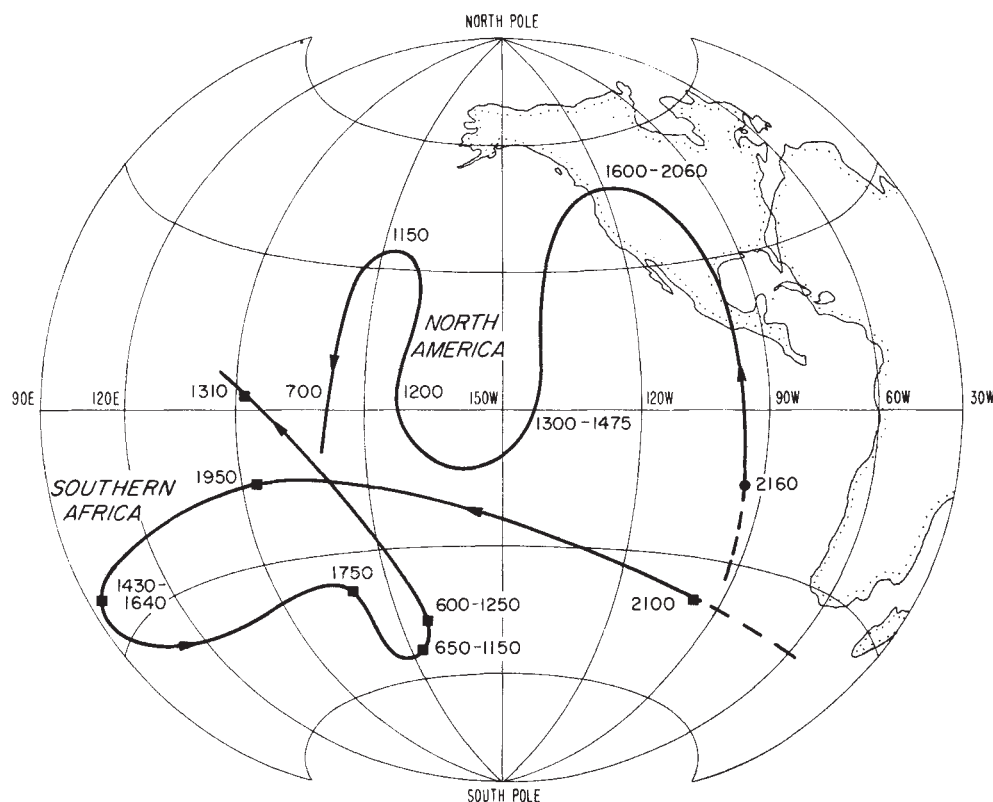


to be defined. I have put forward a pole path for North America for the interval 1,000–2,500 m.y. which was based primarily on sets of isotopically dated igneous rock units⁶. This path was generally supported by data from sedimentary rocks but was in part inconsistent with data from iron formations. This agreement among poles from widely spaced parts of the Canadian and American shields, representing the interval 1,000–2,500 m.y., carries the implication that much of North America has always been a single crustal plate. There is geological evidence, however, that the Canadian shield may have formed

by welding of several plates^{5,11}. Subsequent detailed studies^{12–15} have not contradicted the basic outline of that pole path, although they have provided insight into its finer detail. In particular the study by Fahrig *et al.*¹⁴ suggests that the younger limit of the North American Precambrian curve as it presently exists is better defined as about 700 m.y.

A computer fit of the continents around the North Atlantic¹⁶ and subsequent seafloor spreading evidence¹⁷ suggest that a single giant continent existed at the end of the Palaeozoic. It is thus of immediate interest to test whether the North American

Fig. 2 Result of rotating the Precambrian pole path for Southern Africa onto that for North America according to the computer fit of Bullard and others¹⁶. Ages are in million years.



and Southern African Precambrian pole paths can be superimposed to see whether this single plate also persisted throughout the Precambrian. The pole paths before reconstruction are shown in Fig. 1. The most detailed part of the North American curve is the interval about 700 to 2,000 m.y.: that for Southern Africa is in the interval 1,310–1,950 m.y. (poles P5 to P12 of ref. 7). African poles older than this are determinations from single age points (poles P1 to P4 and the path Fig. 1b of ref. 7). Until the latter are confirmed isotopically and palaeomagnetically, it is perhaps safer to restrict comparisons to the more detailed part of the pole paths between 1,000 and 2,000 m.y. Nevertheless it is interesting that a large polar shift (over 80° of arc) is required to link both the North American and African poles of age about 2,000 million years with those from older rocks; this synchronous shift may be indicative of polar wandering rather than continental drift.

Using a pole of rotation at 14.0° W, 67.6° N to swing Africa against North America¹⁶, the two pole paths for the interval back to about 2,000 m.y. were compared using the program HYPERMAP. The pole paths after rotation are shown in Fig. 2. Using a rotation of 74.8° (ref. 16) there is no superposition of the Precambrian pole paths when Africa is brought up against North America. In fact it is obvious that the shape of the two pole paths is quite different, and that there is little semblance of overlap. There are three possible explanations for this.

The North American pole path proposed by me may not be correct. Although this summarizes more than 100 individual poles from rock units collected over a large area of Canada and the United States, many are from the same time interval, and some poles which define critical parts of the pole path are from rock units whose isotopic ages may yet prove to be preliminary. A particular feature of the African pole path is the loop which begins at about 1,950 m.y. and crosses the pole path again before 1,310 m.y. (ref. 7). Such a loop is not present in the North American pole path, unless the apparent ages of several rock units from different locations are proved to be isotopically too young.

Alternatively, the Southern African pole path may not be representative of the entire African Precambrian shield⁷. It may only be relevant to the Rhodesian and Transvaal cratons. In this case some further rotation would be required to bring the Southern African and North American shields together. But until palaeomagnetic data are available from other cratons in Africa, little can be said about whether Africa was formed by welding of several crustal plates or by accretion onto a single plate.

If neither of these possibilities is correct, we are left with the highly tentative conclusion that there was independent drifting of Southern Africa and North America during the Precambrian. At present all we are justified in saying is that the Precambrian pole paths which have been presently constructed for Southern Africa and North America cannot be superimposed, so they do not at present support the suggestion by Dearnley¹⁸, using orogenic fold belts, and by Hurley and Rand¹⁹, using isotopic evidence, that the ancient crustal nuclei remained intact until the episode of Mesozoic drift. When further data become available, it may be more realistic to obtain the relative positions of the two shields during the Precambrian, by matching the pole paths over restricted time intervals, rather than try to match the entire pole paths.

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Was the Hercynian Orogenic Belt of Europe of the Andean Type?

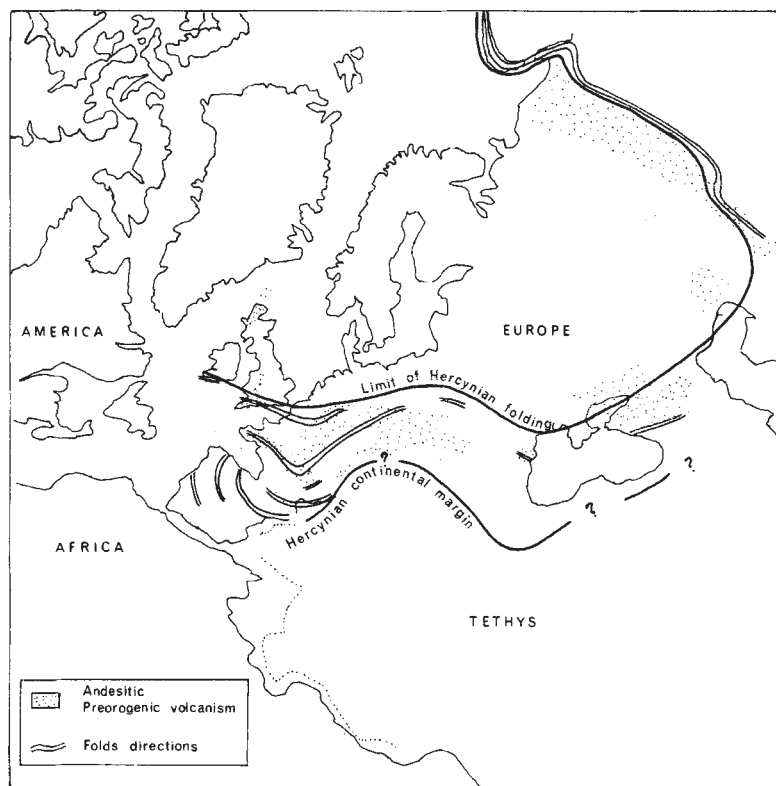
THE Hercynian orogenic belt has distinctive features with regard to the preceding and subsequent orogenies, as demonstrated by Zwart¹ and others². It appears to have formed on a continental basement. There is no evidence for a large eugeosyncline, but rather small subsiding basins or troughs with a shallow type of sedimentation. It is characterized by clastic volcano-sedimentary formations often represented in the Culm facies, pointing to a chiefly submarine or aerial intermediate and acid volcanism of explosive style. From North Britain to the Urals, they form an almost continuous belt (Fig. 1) which could have been a line of volcanic eruptions, active from late Devonian till the end of the lower Carboniferous. The syn- or post-tectonic magmatism is emphasized by intensive granitization (granites and granodiorites) which are, in turn, followed by rhyolitic volcanism during the Permian. The Hercynian metamorphism is rather weak, usually covering the green schist facies and reaching locally the amphibolite facies in the low pressure high temperature series. The tectonic style as it is best observed in the external northward zones appears to be the result of weak compressions and, in contrast, of block faulting which might be partially responsible for passive shear folding in the sedimentary cover, with axial planes parallel to the faults in the basement.

All these features are very distinctive and different from the Alpine model. They are, however, surprisingly similar to those displayed by the Andean Cordillera. Descriptions of this belt^{3–5} stress the importance of the following points: a crystalline basement; pre-orogenic and syn-orogenic andesitic volcanism in rapidly subsiding basins or on temporarily emerged surfaces; intensive granitization (granodiorites) ranging in age from Upper Cretaceous to Oligocene or Miocene together with volcanic activity. The tectonic styles of the Peruvian Andes and of Hercynian Europe are similar as illustrated by the cross sections of Fig. 2. In the external zone again, the tectonic style is considered as generated by block faulting in the basement with passive deformation in the sedimentary cover; the metamorphism is weak or lacking⁶.

Modern ideas of global tectonics revive Suess's concept⁷ of a contrast between the belts resulting from the collision of two continental crusts (Alpine-type or bi-marginal type) and those formed parallel to the margin of an ocean (Andean-type

¹ Bird, J. M., and Dewey, J. F., *Geol. Soc. Amer. Bull.*, **81**, 1031 (1970).

Fig. 1 Hercynian Europe. The fit of continents is from Bullard *et al.*²⁵ and from Smith¹².



or mono-marginal type)^{8,9}. The latter are the result of oceanic lithosphere consumption near the foot of the continental rise along a Benioff plane inclined towards the continent. Deep seated fusion of oceanic materials underthrust along this plane would feed the volcanism and cause high temperature metamorphism and associated granitization in the crust.

If the analogy between the Hercynian and the Andean belts is significant, it must be concluded that the Hercynian belt also developed on a continent along an ocean margin. Relying on considerations from global tectonics theory, the approximate position of this margin can be tentatively inferred. The

ophiolite and blue schist metamorphism line follows the suture between two plates, one of them at least being continental¹⁰. Another inference from the theory is that such a line can be altered by events subsequent to its continental accretion, but cannot be swallowed in a subduction zone and cannot disappear, except perhaps by the oceanization process invoked locally for the western Mediterranean¹¹. The Alpine orogeny culminated with the collision between the continental plates of Eurasia and Africa and was probably preceded by subduction or obduction of the Tethyan plate along the European continental margin. It drifted against that margin fragments of ocean

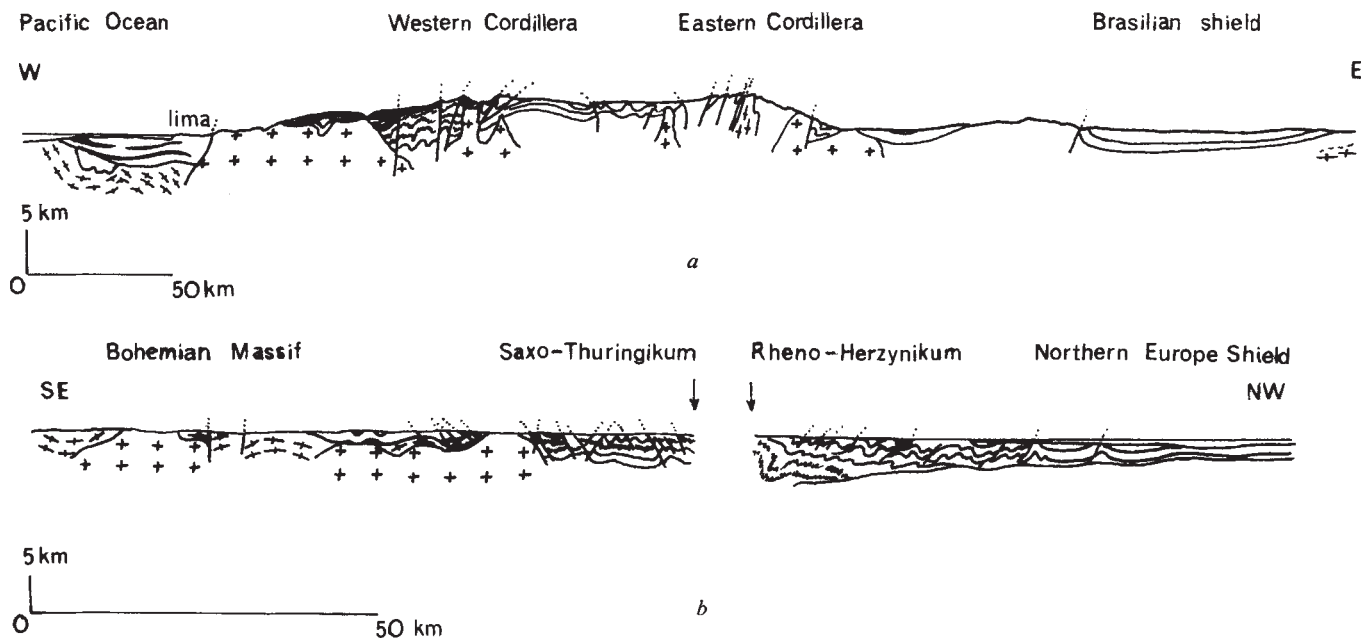


Fig. 2 Comparison between Andean (a) and Hercynian (b) orogenic styles. Profile a: Peruvian Andes, simplified from Megard⁵. The represented folded strata are Mesozoic and Tertiary formations. The underlying blanks are for Palaeozoic formations; the crosses for Cretaceous and Tertiary intrusives; the flattened crosses for Pre-Cambrian gneisses and granites. Profile b: Hercynian Europe from the Netherlands to north-west of the Bohemian Massif. It has been drawn, by juxtaposition of two distinct profiles, from ref. 24. The represented folded strata are Palaeozoic; the crosses Hercynian granites and the flattened crosses Pre-Hercynian metamorphic complexes.

floor represented by ophiolites ranging in age from Jurassic to Eocene and locally submitted to blue schist metamorphism. The problem consists in showing that one branch of the Alpine blue schist-ophiolite line is, at least partially, superimposed on a Hercynian one. In other words, an Alpine continental plate margin is, at least partially, superimposed on the Hercynian continental margin under investigation. Unless there has been rifting and dismembering of the Southern European continent during the Mesozoic, the Hercynian margin would coincide with the northernmost branch of the Alpine ophiolite line. Smith¹² also considers this line as representing the pre-Alpine Tethys margin. It appears to be so in the Greek and Yugoslavian Alps. There the ophiolite line coincides with the limit between the Dinaric and the Alpidic branches of the Alpine system, and it has been demonstrated¹³ that in the former branch the Carboniferous-Permian is continuous and oceanic whereas in the latter it is continental. The spreading age of those ophiolites has been a subject of controversy. The ages were considered as ranging from Jurassic to Eocene^{14,15} like most parts of the Mediterranean Alps. Recently it has been shown that ophiolites of different ages could constitute the belt and Lower to Middle Triassic ages are reported^{16,17}. They are presumably connected with plate activity older than the Alpine one¹². The same might hold true regarding the age of some of the blue schists. Coleman (personal communication) reports that this metamorphism locally affects Palaeozoic rocks whereas nearby Mesozoic diabases and cherts have been subjected to the zeolite facies. The blue schist metamorphism may have been restricted to the more deeply seated Palaeozoic formations; it may simply be of Palaeozoic age.

In the Western Alps some evidence exists of Palaeozoic ophiolites, both in external¹⁸ and internal zones¹⁹. In the latter, Hercynian blue schist metamorphism has been locally reported²⁰ in areas where the Alpine blue schist metamorphism affects the Mesozoic ophiolites²¹. Taking into account this evidence and other palaeogeographic data²²⁻²⁴ the Hercynian margin of the European continent is tentatively considered as extending roughly east to west from the Western Alps towards Greece, and probably beyond through the Caucasus and the Caspian Sea where it would bend to run along the Urals (Fig. 1). From a geometrical reassembly supported by palaeomagnetic and geological evidence, Smith¹² comes to a similar conclusion and points to an open Tethys bounding the Hercynian European continent somewhere along the Northern Alpine belt. In Fig. 1, this reassembly together with that of Bullard *et al.*²⁵ is adopted for the Mediterranean Basin and inspires the drawing of the margin.

Creer's synthesis of palaeomagnetic data²⁶ suggests that the relative positions of America, Africa and Europe might have been nearly permanent inside the supercontinent of Pangea through Palaeozoic times, but does not exclude some reversible plate movements between them. These might have resulted in the Hercynian belts of the Appalachians, of the Atlas and in the particular pattern of Hercynian folding in Spain. The belts would illustrate the bi-marginal type of orogenesis. They will not be dealt with here.

The Hercynian cordillera of Europe would develop with a width of about 1,000 km. The fold axes run roughly parallel to the presumed continental margin (Fig. 1); so does the andesitic volcanic belt, with a distinct inland extension which again conforms with the Andean model. It must be emphasized that this belt, again as its Andean model and its Uralian extension²⁷, does not represent a volcanic island arc because it lies on, and is bounded on the south by, an older continental basement. Northward lies the foreland basin of Northern Europe where the Upper Palaeozoic formations are not folded and rest on a complex basement of Pre-Cambrian shields, welded together by the Caledonian orogenesis. Again the limit of the folding (Fig. 1) is parallel to the other structures.

The Urals present a special case in the sense that the seafloor descending beneath the European continent at the end of the

Palaeozoic resulted in a continental collision with Asia²⁷. In this regard the presence of ophiolites and the occurrence of blue schist metamorphism within this belt²⁷ are noteworthy since they are considered as typical of plate collision¹⁰.

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Archaeomagnetism in Iran

ONE of us (M. T.) has proposed that the archaeomagnetic method of dating be used to examine a number of Iranian

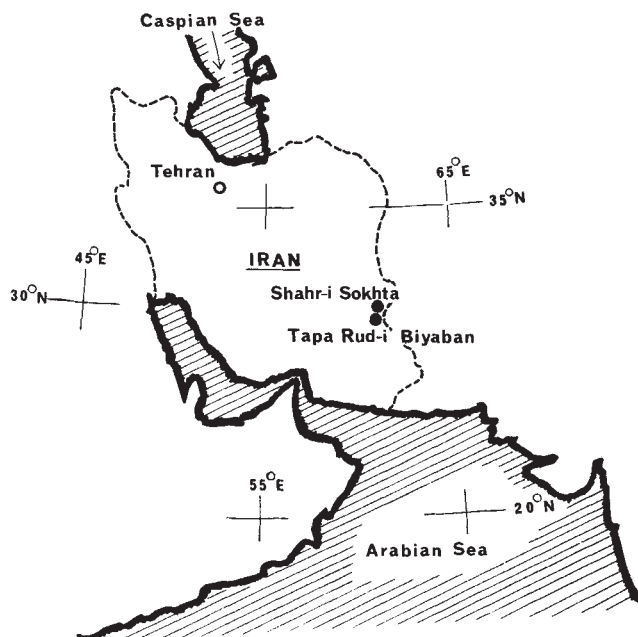


Fig. 1 Map of Iran. Solid circles show sampling sites.

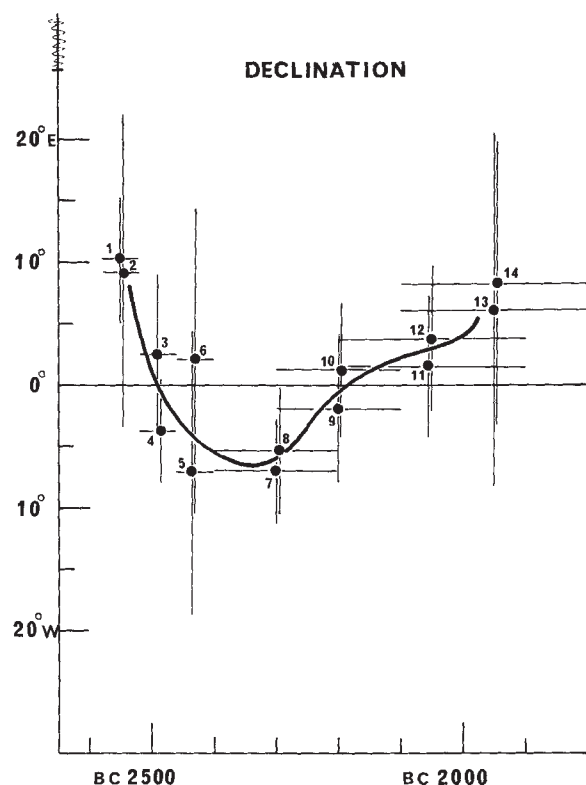


Fig. 2 Change of the geomagnetic declination.

baked earths in the Istituto Italiano. This information was sent to Japan by Aitken, leading to a cooperative programme involving the Istituto Italiano and the Universities of Oxford, Kyoto and Osaka. The first trip to collect the baked earths (see Fig. 1) was made in October 1971.

From the kiln sites and other fireplaces excavated in eastern Iran more than 400 baked earths were orientated *in situ*, removed from the ground and then transported carefully to Osaka University where we determined the respective remanent magnetic vectors, using a sensitive astatic magnetometer. This method is in principle the same as those used by geophysicists to study palaeomagnetism¹⁻³. We present here, the preliminary results of our measurement.

The remanent vectors of the baked earths, when arranged

in their chronological order, were seen to follow a systematic pattern so that we could confidently trace the past magnetic field as shown in Figs. 2 and 3. The dates when the soils were fired can be estimated relatively accurately by establishing cultural parallels in other archaeological remains associated with the baked earths⁴. It is reasonable therefore to assume that this change represents the secular variation in Iran from 2500 BC to 2000 BC.

The results are also tabulated in Table 1 in which D , I , k and θ are the declination, the inclination of the remanent magnetism, the precision factor⁵ and the cone angle of 95% confidence, respectively.

The vertical line drawn at each point of observation in the figures is the error angle of the measurement, and the hori-

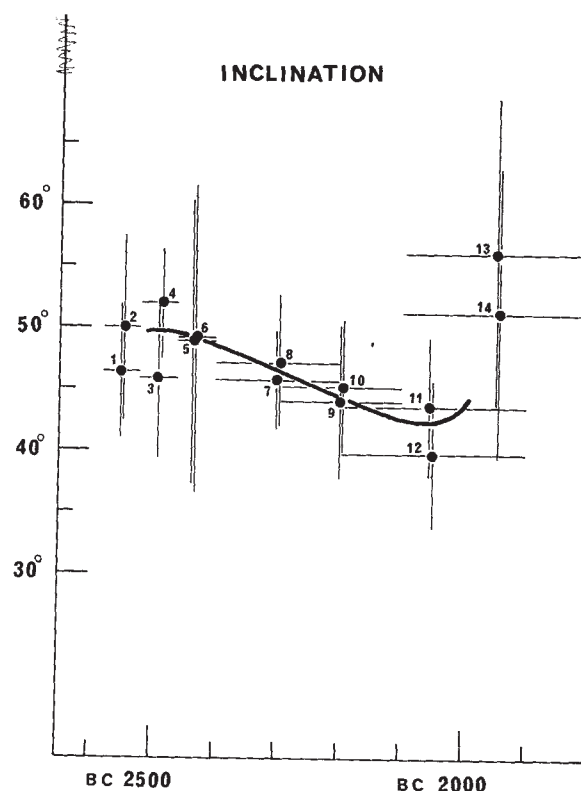


Fig. 3 Change of the geomagnetic inclination.

Table 1 Data on the Remanent Magnetism

Site	Locality	N	D (°E)	I (°)	k	θ (°)	Type
Period II (2700-2400 BC)							
1 XLIX	Shahr-i Sokhta	7	10.3	46.4	131.0	5.3	Kiln
2 XXV	Shahr-i Sokhta	6	9.1	50.0	30.1	12.4	Fireplace
3 XXIV	Shahr-i Sokhta	11	2.5	49.9	44.3	6.6	Fireplace
4 CCI	Shahr-i Sokhta	5	-3.8	52.0	293.0	4.3	Oven
5 XLIX	Shahr-i Sokhta	9	-7.1	48.9	21.5	11.4	Oven
6 XLVII	Shahr-i Sokhta	8	2.2	49.2	20.7	12.5	Oven
Period III (2400-2200 BC)							
7 TRB ₂ /F ₄	Tapa Rud-i Biyaban	11	-6.9	45.7	107.1	4.2	Kiln
8 TRB ₂ /F ₂	Tapa Rud-i Biyaban	17	-5.2	47.2	49.0	5.2	Wall of chamber
Period III and IV							
9 TRB ₂ /F ₃	Tapa Rud-i Biyaban	13	-1.8	44.1	49.5	6.0	Kiln
10 TRB ₂ /F ₁	Tapa Rud-i Biyaban	19	1.3	45.2	36.4	5.6	Kiln
Period IV (2200-1800 BC)							
11 CXLIV	Shahr-i Sokhta	8	1.6	43.7	96.4	5.7	Fireplace
12 CXXXVII	Shahr-i Sokhta	13	3.7	39.7	50.8	5.9	Kiln
13 CXXXVII	Shahr-i Sokhta	6	6.1	56.1	15.0	17.5	Oven
14 CXXXVIII	Shahr-i Sokhta	7	8.3	51.3	27.6	11.7	Fireplace

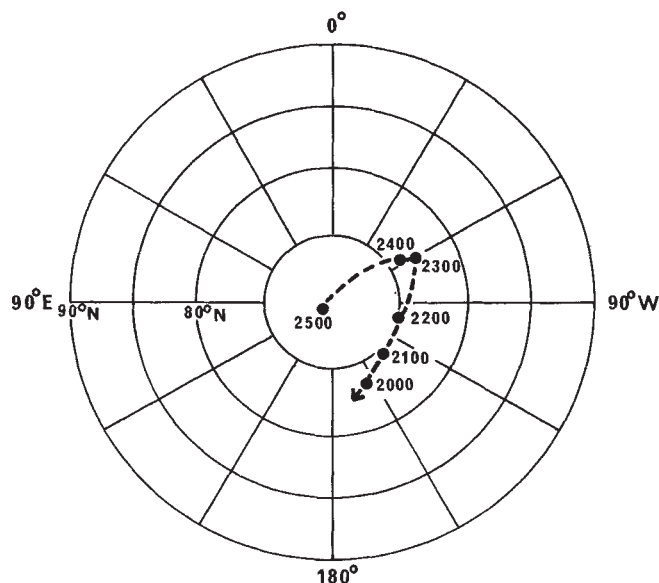


Fig. 4 Path of virtual pole positions.

zontal line the age uncertainty of each baked earth. The path of virtual pole positions derived from our calculation is shown by the smooth curve in Fig. 4. The period required for complete rotation of the clockwise loop in the path is approximately 500 years. Similar clockwise loops have been observed in Japanese^{6,7} and North American⁸ archaeomagnetic data^{6,7}. In both cases, however, more recent baked earths less than 2,000 years old were dealt with. Nevertheless the period of the looping motion was also 500 years. This difference of the Iranian secular field from the field in other parts of the world may represent only the behaviour of the Earth's magnetic field.

The magnetic charts now being prepared from these data may be used as an archaeometric standard with which to date other remains from this part of the world.

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Rate of Solution of Gaseous Sulphur Dioxide at Atmospheric Concentrations

Liss¹ has calculated the rate of exchange between sulphur dioxide and environmental water. We report here experimental work which verifies the results of his calculations. The rate

of solution of SO₂ at 20° C was examined by passing a non-laminar flow of air (bulk velocity ~1.5 cm s⁻¹) and ³⁵SO₂ at concentrations around 300 μg m⁻³ over stirred sodium perchlorate solutions. The pH values of these solutions were adjusted by addition of sodium hydroxide or perchloric acid because ionic strength exerts little effect on rate of uptake. Oxidation of the sulphur (IV) anions in sodium perchlorate solution is small over the time scale involved (unpublished data of P. B.).

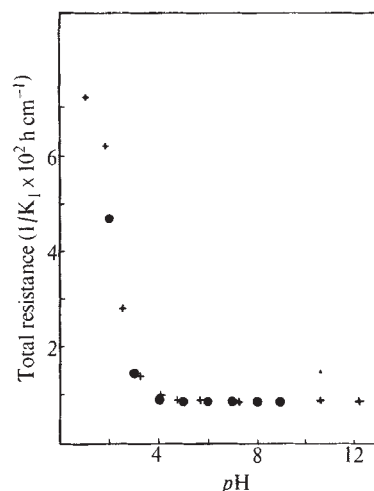


Fig. 1 A comparison of experimental and calculated values of total resistance. ●, Liss¹; +, experimental.

The total concentration of sulphur species in solution was determined by liquid scintillation counting of the aqueous solution. The uptake rate and pH remained constant during each experiment (1,000 s). Values calculated from these experimental measurements were expressed as resistance on a liquid concentration basis (1/K₁). This total resistance was also determined from Liss's data using Danckwerts's equation², where 1/k₁ and 1/k_g are the liquid and gas phase resistances and H is the Henry's law constant.

$$1/K_1 = 1/k_1 + 1/Hk_g$$

The excellent agreement between experimental and calculated values is shown in Fig. 1.

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BIOLOGICAL SCIENCES

Human Brain Monoamine Oxidase: Multiple Forms and Selective Inhibitors

It is well recognized that monoamine oxidase (monoamine: O₂ oxidoreductase (deaminating), EC 1.4.3.4) (MAO) plays an important role in the degradation of biologically active monoamines in the brain^{1,2}. There is much evidence pointing to changes in monoamine metabolism in mental illnesses

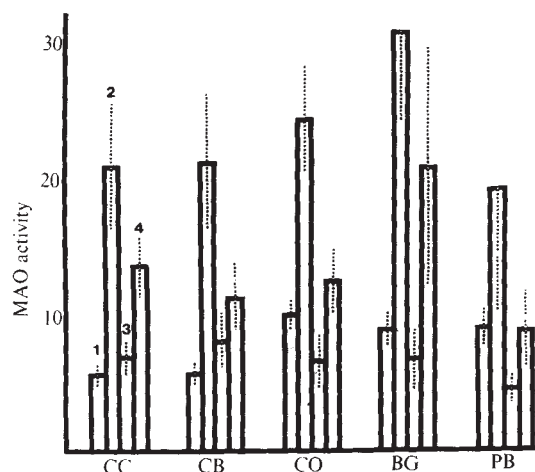


Fig. 1 Distribution of mitochondrial MAO activity (mean $\pm$ s.e.) in different anatomical areas of brain from ten untreated (control) subjects. Substrates: 1, kynuramine; 2, tyramine; 3, tryptamine; 4, dopamine. Anatomical areas: CC, cerebral cortex; CB, cerebellum; CO, centrum ovale; BG, basal ganglia; PB, pineal body.

characterized by alterations in mood^{3,4}. Perhaps the most important property of MAO inhibiting drugs is their ability to bring about a lightening of affect in depressed patients⁵. That this effect results solely from the inhibition of MAO has not been widely questioned, although the antidepressive effect is not shared to an equal extent by all drugs in the group⁶. An attempt has been made to explain this finding in terms of differing ability of the MAO inhibitors to prevent amine reuptake⁷; however, it has seemed to us that an explanation might better be sought in terms of differential inhibitory capacity of these drugs on the four molecular variants of MAO in the human brain⁸.

The single relevant set of data so far published describes some *in vitro* observations⁹. Because certain observations made during an *in vivo* study of MAO inhibitors in the rat¹⁰ suggest that the existence of the multiple forms, with their special properties, is more than a test tube phenomenon, it seemed desirable to try to obtain some direct evidence for their *in vivo* existence in the human brain. The practice of treating depressive illness in geriatric subjects with MAO inhibitors gave us the opportunity of making some sighting observations on fresh autopsy material from patients being treated with different drugs in this group.

Brains were obtained within 12 h after death from patients aged between 70 and 92 yr, who had been treated with tranlylcypromine (30 mg daily), clorgyline (20 mg daily) or isocarboxazid (30 mg daily) in divided doses in an attempt to alleviate their depressive illness. Control brains were obtained from patients of a similar age range from the same hospital who had not been treated with MAO inhibitors. Other medications were given as required. There were ten subjects in each group and ten in the control group. Samples from each brain were taken from cerebral cortex, cerebellar cortex, centrum ovale, basal ganglia and pineal body and frozen at -20°C until required. Mitochondria from each of these regions were isolated by differential centrifugation¹¹, and their MAO activity measured using kynuramine¹², ^{14}C -dopamine, ^{14}C -tryptamine and ^{14}C -tyramine¹³ as substrates. Protein nitrogen was estimated¹⁴ using bovine serum albumin as standard. These procedures were also used to assay MAO activity of constituent isoenzymes isolated from pooled mitochondria from basal ganglia or cerebral cortex of treated patients and controls. Enzyme was solubilized by the combined use of sonic oscillation and a non-ionic detergent¹⁵ and purified as previously described¹⁶. Separation into four different bands of activity was then achieved by polyacrylamide gel electrophoresis¹⁶; three (MAO_{1-3}) migrated from cathode to anode and one (MAO_R) from anode to cathode.

Whole mitochondrial MAO activity from control subjects is shown in Fig. 1. The highest values were observed in samples prepared from basal ganglia and centrum ovale; of the four substrates used, tyramine was most readily deaminated. These data are in general agreement with our earlier findings on human brain mitochondria⁹.

In Fig. 2, mitochondrial MAO activity measured in the five chosen brain areas of patients pretreated with clorgyline, isocarboxazid or tranlylcypromine is expressed as "percentage inhibition", being the ratio of test to control values. Because we were dealing with clinical material from patients who, inevitably, were on individual dosage schedules for differing periods of time, the scatter of results is large. Even so, certain trends are clear; after treatment with isocarboxazid, for example, the oxidation of tryptamine and dopamine was consistently inhibited less than that of kynuramine and tyramine. After tranlylcypromine, on the other hand, dopamine metabolism was inhibited to a greater extent than that of the other substrates investigated. These findings were noted in all anatomical areas investigated. Clorgyline pretreatment, however, resulted in wide variation with regard to both degree of substrate oxidation and anatomical area: no inhibition was

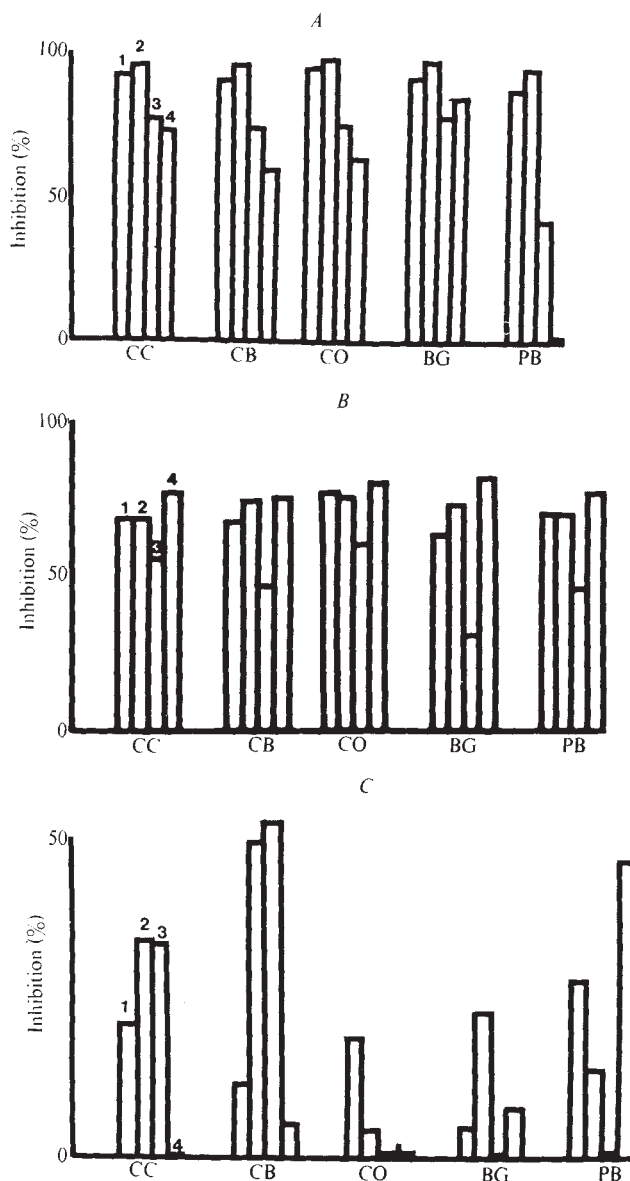


Fig. 2 Mitochondrial MAO activity in brains from human subjects after treatment with (A) isocarboxazid, (B) tranlylcypromine, and (C) clorgyline. Substrates and anatomical areas as in Fig. 1.

Table 1 Effect of Inhibitor Pretreatment on MAO Isoenzymes of Human Basal Ganglia and Cerebral Cortex

	Clorgyline		Tranlycypromine		Isocarboxazid	
	BG	CC	BG	CC	BG	CC
Kynuramine						
MAO 1	40	37	80	78	92	92
2	40	45	100	95	94	95
3	15	30	86	70	27	20
R	0	0	50	60	5	23
Tyramine						
MAO 1	20	17	89	95	86	85
2	0	21	78	77	86	85
3	30	35	14	15	13	23
R	0	11	0	0	10	7
Tryptamine						
MAO 1	20	10	100	60	87	90
2	0	17	81	87	70	92
3	0	0	20	27	43	33
R	0	0	11	13	20	20
Dopamine						
MAO 1	12	5	47	45	50	55
2	14	13	51	50	61	75
3	20	0	33	40	13	18
R	5	0	28	25	0	15

The results are expressed as percentage inhibition of treatment samples compared with untreated controls. Mitochondria from ten different brains in each test group and from the control brains were pooled prior to separation of isoenzymes (see text). All observations were made in duplicate. BG, basal ganglia; CC, cerebral cortex.

observed, for example, in the pineal body, basal ganglia and centrum ovale when tryptamine was used as substrate, whereas a greater than 50% reduction in cerebral cortex MAO activity was recorded; however, when dopamine was the substrate, clorgyline pretreatment reduced activity in the pineal body by almost half, while the cerebral cortex was unaffected.

The effect of the three inhibitors on activity of multiple forms isolated from basal ganglia and cerebral cortex, using four different substrates, is shown in Table 1. The various isoenzymes are not inhibited to the same extent by any of the inhibitors. In tissues from both areas, for example, tyramine, tryptamine and kynuramine oxidation by MAO₁ and MAO₂ was reduced by about 90% by tranlycypromine and isocarboxazid. MAO₃ was inhibited to a much smaller extent by these drugs and the pattern was less consistent. Tranlycypromine was the only drug having any marked inhibiting effect on MAO_R and then only when kynuramine and, to a lesser extent, dopamine were used as substrates. The inhibitory effect of clorgyline on MAO₁₋₃ could be demonstrated best using kynuramine as substrate but barely at all with dopamine or tryptamine. A comparison of whole mitochondrial activity with that of the individual isoenzymes, using different substrates, shows good agreement. Tranlycypromine, for example, the most effective inhibitor of mitochondrial dopamine oxidation (Fig. 2b), was the only drug to cause a reduction of dopamine or kynuramine oxidizing activity in the dopamine specific MAO_R. Clorgyline, with its more highly substrate-dependent mitochondrial inhibition pattern (Fig. 2c), showed a similar variability with regard to the multiple forms; it did not turn out to be a specific inhibitor of any one isoenzyme.

Many chemical compounds¹⁷, otherwise quite dissimilar, fall empirically into a single group on the basis of their ability to inhibit MAO. Many members of this group are able to bring about a lightening of affect when administered to human subjects. The clinical response could not unreasonably be explained as a consequence of the intrinsic MAO inhibition property itself rather than some secondary effect of the compound such as its ability to block amine re-uptake⁷.

The therapeutic effectiveness of MAO inhibitors is likely to rely on the accumulation of a particular amine substrate at a specific site in the brain⁹. Complementary experiments to

ours here in which dopamine, noradrenaline and 5-hydroxytryptamine were measured at different brain sites on the same clinical material have been carried out (A. B. B. J., C. M. B. P., W. J. N., K. Price, and R. S. Stacey, unpublished work). Although the data tend to support the thesis that clinical improvement is bound up with MAO inhibition, too few observations were made to allow firm conclusions to be drawn.

We have adopted an alternative approach to the problem. By mapping brain MAO according to its isoenzymes, their substrates and inhibitor specificities, we hope to pinpoint sites with particular substrate preferences, and eventually be in a position to tailor specific inhibitors, therapeutically effective in depression, yet without the occasional dangerous side-effects inherent in conventional "blunderbuss" MAO inhibitor therapy¹⁰. Clorgyline with its differential inhibitory effect¹⁸ provides a firm precedent for the type of compound we seek, although clorgyline retains the most serious side-effect of the group by interfering with tyramine degradation¹⁹. Thus patients eating cheese or other substances with a high tyramine content²⁰ are liable to a sudden and dangerous rise of blood-pressure^{21,22}.

One particular problem of this type of work is to harvest sufficient isoenzyme for detailed study. Because of the unique electrophoretic characteristics of MAO_R, it is possible to scale up our preparative procedure by continuous flow electrophoresis. As MAO_R seems to be a specific dopamine oxidizing enzyme in its own right²³, the data obtained will have to be interpreted cautiously.

Although the present data are suggestive many further observations are needed before a true intracellular function can be assigned to the MAO isoenzymes, and they can be shown to be rather more than a complex artefact. Technical problems⁹ have so far made it impracticable to use 5-hydroxytryptamine and noradrenaline as substrates and clinical circumstances have similarly ruled out the possibility of correlating therapeutic benefit with biochemical change. If these gaps can be filled we may be on the way to solving some of the outstanding problems posed by depressive illness.

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Separation of the Sinusoidal Components of the Human Electroencephalogram

THE nature of the sinusoidal cortical activity in man, particularly the alpha rhythm first explored by Berger¹, remains obscure. Andersen and Andersson², among others, consider the alpha rhythm to be the result of summated post-synaptic potentials largely under the control of recurrent inhibitory thalamic networks. From a theoretical viewpoint Wiener³ suggested that the alpha rhythm could be produced by a population of coupled non-linear oscillators. Some preliminary results, based on four normal human subjects, of a method of separation of EEG components are reported here. They provide new information about these concepts and also on the nature of the "after discharge" of the averaged visual evoked response as well as its relationship to the primary components of the waveform.

The first stage of the analysis, using a Micro 16 digital computer and a fast Fourier transform algorithm, involves passing the data through a set of wideband frequency selective filters. The outputs of these are measured every 1/256 s and the mean spectra computed. These mean spectra are then plotted one below the other to give a three dimensional effect. This is illustrated in Fig. 1 for an averaged visual evoked response, where the alpha band (near 10 Hz) component appears to have split into two parts some 200 ms after the flash. By 300 ms it seems that the two components have recombined, possibly with the higher frequency one undergoing subsidiary splitting; and by 400 ms the alpha band activity is re-established in a stable form.

To examine these fluctuations in greater detail, a second stage of analysis is necessary. This makes use of the phase information in successive pairs of the previously computed transforms. Although complicated in practice the principle of the method used is straightforward. It depends on the fact that, if the frequency and phase of a sinusoid are known at time T_1 , it is possible to predict what the phase will be at some future time T_2 . If this prediction is found to be in error, then the frequency of the sinusoid will have changed. The direction of frequency change, increase or decrease, is derived from the sign of the error in the predicted phase. This technique of tracing fre-

quency changes can be effected by means of two equal frequency filters which overlap in time (Fig. 2). The phase of the signal is measured by the first of these filters and is used to predict the phase that will be measured by the second. The frequency of

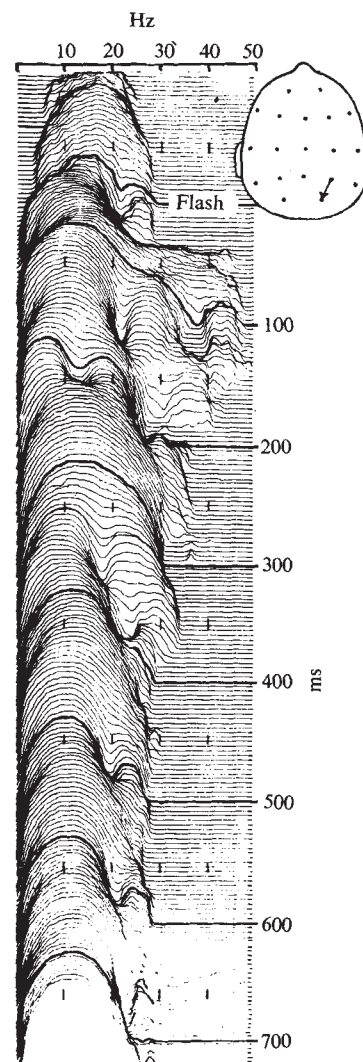


Fig. 1 Successive mean spectra of an average evoked response to random photic flash stimulation. The spectra are computed at 0.5 Hz intervals along the frequency axis and at 1/256-s increments along the time axis. A logarithmic amplitude scale is used. The filter length was 156 ms, having a $\frac{1}{2}(1 + \cos \omega t)$ Hanning envelope¹⁰. Frequencies below 5 Hz have been progressively attenuated and amplitudes below an arbitrary level are not resolved, so producing the flat areas. (The response plotted here is illustrated at the top of Fig. 3.)

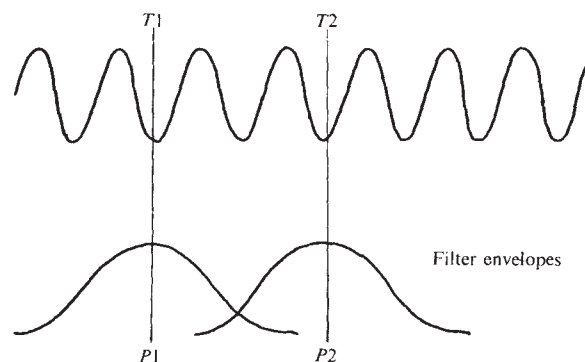
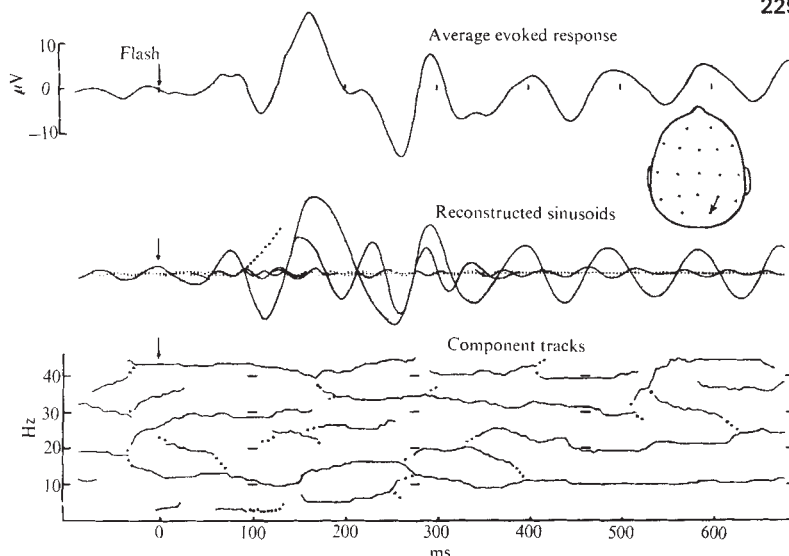


Fig. 2 Basic principle of the method of frequency component tracing. The phase of a signal at time T_1 relative to filter P_1 is used to predict the phase at T_2 relative to filter P_2 . Comparison of actual with predicted phase at T_2 is used to detect the position of a component.

Fig. 3 Top: averaged visual evoked response from an occipital electrode placement as a result of sixty-four random light flash stimuli at intervals from 1–5.5 s. Eyes closed. Middle: some of the reconstructed sinusoidal components. The scale is slightly different to that of the top trace. Bottom: the frequency-time tracks derived by the method described in the text. Filter length 195 ms. Comparison of the reconstructed sinusoids with the original waveform shows how these apparently account for its shape. For example, at 200 ms after stimulus the waveform is constructed mainly from a combination of two components at approximately 5 and 15 Hz whose frequency-time tracks split at about 140 ms and recombine at about 280 ms. The alpha band sinusoid following the response from 400 ms onwards is continuous with earlier sinusoids. In the single evoked response, not illustrated, it is continuous with the pre-stimulus alpha sinusoid although frequency shifts may result in their relative phases being different.



the filters is then modified until the error in predicted phase is minimized, at which point they will have "locked on" to the sinusoid. Thus by moving pairs of such filters through the data it is possible to follow the frequency changes with time of individual sinusoidal components and to plot these in the form of frequency-time tracks. Because the filter outputs give amplitude as well as phase information the sinusoids can be reconstructed as they are tracked. By plotting the frequency-time tracks and the reconstructed sinusoids in parallel with the original signal it can be shown how particular waveforms are constructed from summations of several components (see Figs. 3 and 4).

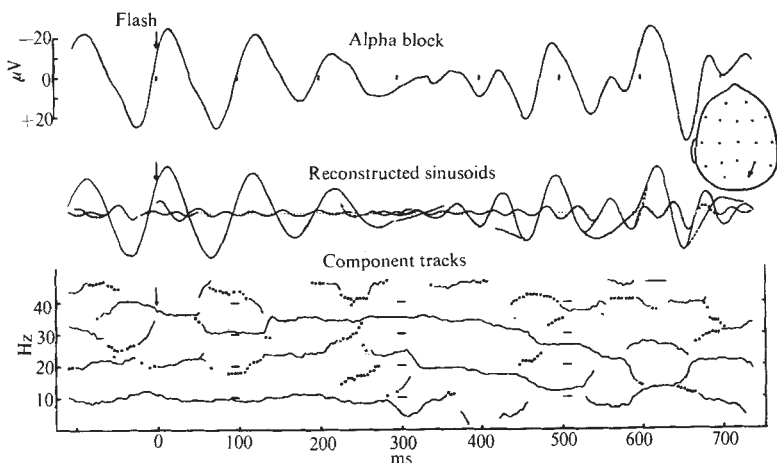
When the technique is applied to an averaged visual evoked response (Fig. 3) the principal components of the waveform are apparently separated and are seen to be produced by the splittings and recombinations of alpha band sinusoids, principally between 100 and 400 ms after the stimulus. This confirms the impression given by the successive mean spectra (Fig. 1). Complex fluctuations are also evident at other frequencies and links may occur between these and the alpha band components. To exclude the possibility that these phenomena could have been produced by the averaging process itself, the method has also been applied to individual responses. Although their form can differ from the average, apparently depending on the signal structure and phasing^{4,5} at the time of stimulus, similar interactions have been observed. Apart from the evoked response, the alpha blocking response in particular (Fig. 4) demonstrates a variety of such inter-relationships between different frequency components and shows that they are a widespread feature of the ongoing EEG.

These results, even though the method does not provide a complete picture of the component tracks, indicate a unity in

the mechanisms involved across all of the conventional frequency bands. They go some way to confirm Wiener's suggestion that alpha activity arises from coupled non-linear oscillatory systems pulling each other into synchrony. However, there is the added feature that clusters of such synchronized components may form at several frequencies, with linking components representing groups of oscillators moving from one cluster to another, for example, a component may be part of alpha one moment and beta the next. It can also be observed that, when a component splits, both parts appear to move away from each other in the manner that one would expect if each cluster were to be formed from the synchronization of non-linear generators of varying natural periodicities. Splitting of a cluster could result from a disturbance of equilibrium produced by the approach of another cluster, or of a stimulus affecting the properties of the generators or of the coupling between them.

Further, it seems from preliminary results similar to those in Fig. 3, that there may be parts in the phase of a sinusoid at which splitting and combination are more likely to occur, implying that the degree of coupling between oscillatory systems depends partly on their phase. This property, together with the tendency of non-linearly coupled clusters to form at frequencies having some simple ratio to one another⁶, would tend to impose a degree of order on the structure of the EEG which would lead to the ability to repeat particular types of waveforms. Phase dependent coupling could be associated with the concept, proposed by Bartley and Bishop⁷, of brain excitability cycles linked to cortical rhythms. Gaarder *et al.*⁸ have shown that fixation saccadic eye movements have a probability of occurrence which is dependent on alpha phase; some workers⁹ have related reaction times to alpha phase. Andersen and Andersson²

Fig. 4 Top: a section of EEG showing an alpha blocking response (from 250 to 450 ms) to a light flash stimulus. Eyes closed. Middle: separated and reconstructed sinusoids. Bottom: frequency-time tracks of the components of the blocking response. Filter length 156 ms. The example indicates extensive component splitting and linking across a wide frequency range and how this apparently produces the irregular shape of the original waveform. The alpha band waves before and after the block are linked and the reduction of alpha amplitude before the block appears to be caused by alpha attenuation as well as splitting. Component linking is also seen to be occurring before the stimulus. The blocking response can vary widely. In some cases the alpha before blocking attenuates to a reduced amplitude alpha during the block but may still have some components linking with it.



consider that multiple interconnected recurrent inhibitory thalamic networks, which could be expected to exhibit phase dependent coupling, are responsible for "pacing" EEG alpha rhythms. If the pacing is as precise as they suggest then each of the components resulting from alpha splitting (as in Fig. 4 during the alpha blockade) could represent a different thalamic rhythm. These results also indicate, however, that alpha waves and activity at other frequencies are not independent. It is possible that phase dependent coupling may be occurring wherever there are fluctuations of neural excitability related to the sinusoids of the EEG. Weiner³ has shown that a property of coupled non-linear oscillatory systems would be self-synchronization without the need for some central pacemaking system. It may therefore be that the thalamic networks form part of the oscillatory systems involved and that, in varying conditions, sections of the oscillatory population may at times have more dominance than others.

In conclusion, the scalp recorded EEG is derived from differences of average cortical activity over relatively large areas. Whether similar phenomena to those demonstrated here also appear at a more localized cortical or even cellular level remains to be seen. Nevertheless the new method of analysis shows that individual components of EEG waveforms can be separated and that ordered structural relationships are present. It is hoped that this development will enable advances to be made in the understanding of these waveforms and of the laws governing their behaviour.

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Binding of EDTA, Histidine and Acetylsalicylic Acid to Zinc-Protein Complex in Intestinal Content, Intestinal Mucosa and Blood Plasma

ETHYLENEDIAMINETETRAACETIC acid (EDTA) added to a diet containing isolated soybean protein has improved the growth rate and reduced the incidence of a hock disorder caused by zinc deficiency¹ in chickens. Furthermore, the addition of histidine and 8 ml. anti-arthritis agents, including acetylsalicylic acid (aspirin), prevented "arthritic-like" leg abnormalities in chickens fed such diets deficient in zinc^{2,3}. Supplementation of the diet with zinc promoted normal growth and feather development, and prevented leg abnormalities, while supple-

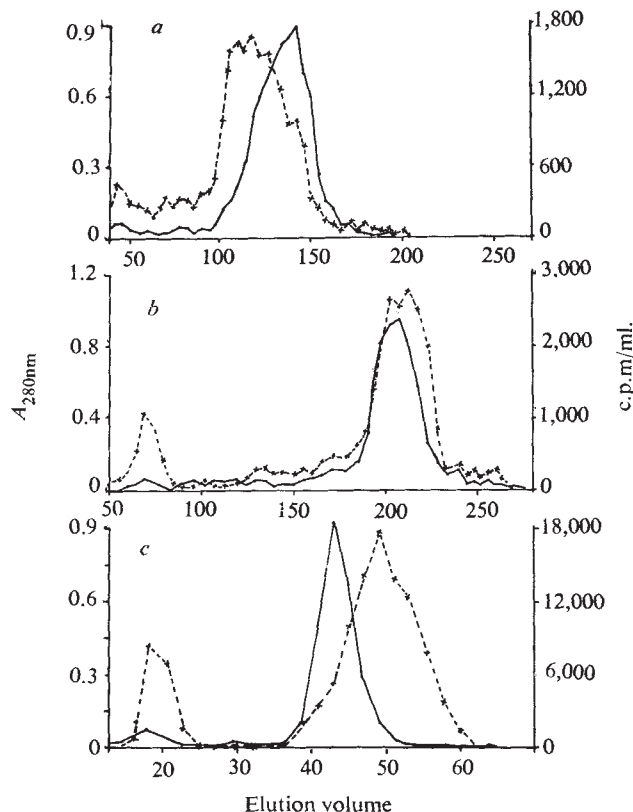


Fig. 1 'Sephadex' gel filtration of samples from three birds dosed orally with ^{65}Zn . Graph was obtained from one bird representative of the three. a, Blood plasma elution 'Sephadex G-150' column. b, Intestinal mucosa soluble fraction elution by 'Sephadex G-150' columns. c, Intestinal digesta preparation elution by a system of 'Sephadex G-50' and 'Sephadex G-10' columns. x --- x, Absorbance; ●—●, ^{65}Zn .

mentation with the anti-arthritis agents had little or no effect on the symptoms of zinc deficiency except the leg defect. Amino-acids, particularly histidine, seem to be involved in the passage of zinc from the intestinal lumen to the blood stream^{4,5}. EDTA was found to bind zinc in the intestinal digesta and seemed to remain bound as it passed through the intestinal mucosa and was transported in the blood plasma, confirming previous work⁵. We have investigated the binding of histidine and aspirin to zinc and their transport from intestinal digesta to the blood stream to find out whether these compounds alleviate the abnormal leg conditions by the same mechanism.

Twelve 2 week old single comb white Leghorn males were divided into four groups of three. Two groups were fed a practical broiler type diet⁶ containing 70 p.p.m. zinc. Groups 3 and 4 received the same diet supplemented with 0.125% EDTA and 1% aspirin, respectively. Diets and water were supplied *ad libitum*. At 2 weeks of age the birds were fasted overnight and then allowed to eat freely for 45 min before they were dosed orally by pipette with ^{65}Zn alone or in combination with ^{14}C -histidine, ^{14}C -EDTA or ^{14}C -aspirin, respectively. Intestinal digesta, intestinal mucosa and blood plasma were prepared as described before⁵. The nature of the binding of ^{65}Zn to histidine, EDTA and aspirin was studied by gel filtration. Distilled water at neutral pH was used as eluant and protein was estimated by absorbance at 280 nm. The presence of ^{65}Zn and ^{14}C -histidine, EDTA and acetylsalicylic acid was determined by counting in a well-type scintillation counter and in a liquid scintillation spectrometer, respectively. The ratio c.p.m. ^{14}C from the different compounds to c.p.m. ^{65}Zn was determined by adding the individual counts of ^{14}C and ^{65}Zn for all samples in the major peaks obtained by gel filtration.

One of the two groups fed the basal diet was dosed with 1 ml. of ^{65}Zn solution (50 $\mu\text{Ci/ml}$. ^{65}Zn carrier-free). The

Table 1 Ratios Obtained from the ^{14}C and ^{65}Zn Counts in Major Peaks eluted in the Histidine and EDTA Studies and in the Whole Elution Material in the Aspirin Study

Ratio	Intestinal digesta preparation	Mucosal soluble fraction	Blood plasma
Major peaks			
^{14}C -histidine: ^{65}Zn	1.50	2.30	3.86
^{14}C -histidine: ^{65}Zn	1.31	2.50	3.36
^{14}C -histidine: ^{65}Zn	3.63	3.95	3.84
^{14}C -EDTA: ^{65}Zn	1.68	1.56	7.00
^{14}C -EDTA: ^{65}Zn	1.67	1.53	1.56
^{14}C -EDTA: ^{65}Zn	1.53	1.64	1.87
Whole elution			
^{14}C -aspirin: ^{65}Zn	1.28	1.17	15.84
^{14}C -aspirin: ^{65}Zn	1.74	2.23	13.90
^{14}C -aspirin: ^{65}Zn	2.35	2.61	9.78
^{65}Zn : μg zinc	2,679.00	1,902.00	1,119.00
^{14}C -aspirin: μg zinc	6,289.00	4,972.00	10,935.00

Each figure represents values obtained for one individual chicken in each group.

intestinal digesta of this group was subjected to gel filtration using a two column system where the effluent of the first column (1.5 cm $\times$ 30 cm) packed with 'Sephadex G-50' entered a second column (1 cm $\times$ 15 cm) of 'Sephadex G-10'. Mucosal soluble fraction and blood plasma were separated by a column (2.5 cm $\times$ 45 cm) containing 'Sephadex G-150' (Fig. 1). Gel filtration of intestinal digesta, mucosal soluble fraction and blood plasma associated ^{65}Zn to major peaks, indicating binding of the metal to amino-acids and proteins as previously reported⁵.

Gel filtration of these preparations from chickens fed the basal diet and dosed with 50 μCi of ^{65}Zn and 3×10^{-4} mM ^{14}C -histidine (specific activity 250 mCi/mmol) showed that ^{65}Zn and ^{14}C -histidine were eluted in the same fractions in all cases (Fig. 2). Although the ratios of ^{14}C -histidine: ^{65}Zn (Table 1) indicated some losses of ^{65}Zn , possibly due to ex-

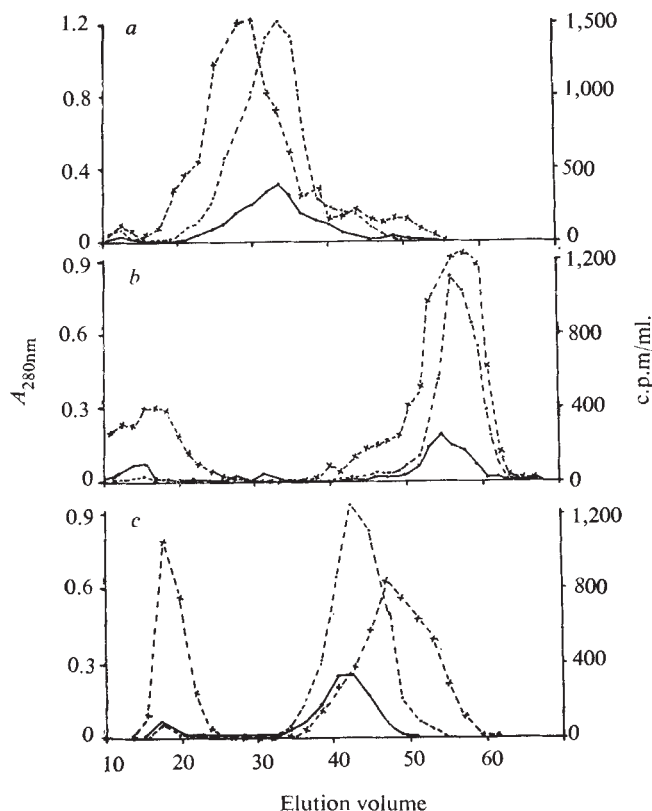


Fig. 2 'Sephadex' gel filtration of samples from three birds dosed orally with ^{65}Zn and ^{14}C -histidine. Graph was obtained from one bird representative of the three. *a*, *b* and *c* as for Fig. 1. $\times$ --- $\times$, Absorbance; $\bullet$ — $\bullet$, ^{65}Zn ; $\bullet$ --- $\bullet$, ^{14}C -histidine.

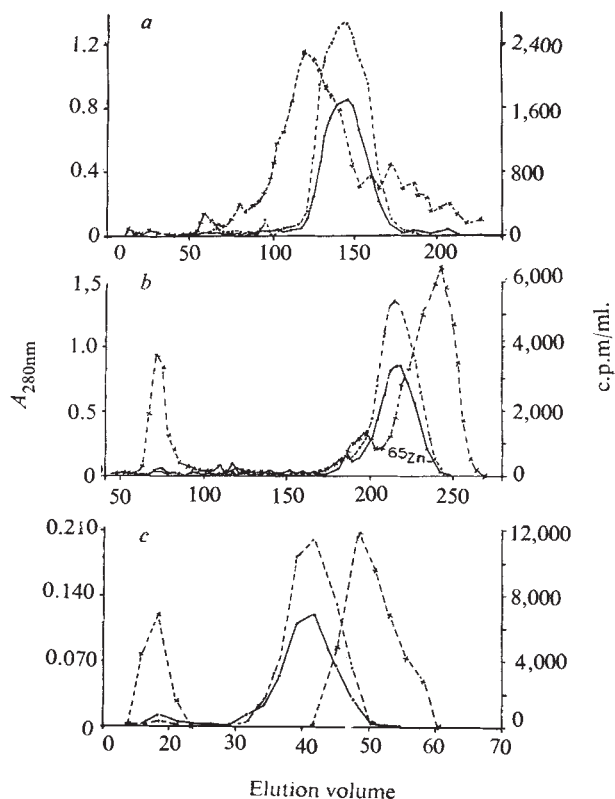


Fig. 3 'Sephadex' gel filtration of samples from three birds dosed orally with ^{65}Zn and ^{14}C -EDTA. Graph was obtained from one bird representative of the three. *a*, *b* and *c* as for Fig. 1. $\times$ --- $\times$, Absorbance; $\bullet$ — $\bullet$, ^{65}Zn ; $\bullet$ --- $\bullet$, ^{14}C -EDTA.

change with the non-radioactive metal, ^{65}Zn was found only when ^{14}C -histidine was present. Histidine forms 1:1 and 2:1 complexes with zinc^{4,7}.

Gel filtration of intestinal digesta, mucosal soluble fraction and blood plasma from chickens fed the basal diet containing 0.125% EDTA and dosed with 50 μCi of ^{65}Zn and 3×10^{-4} mM of EDTA (specific activity 2.10 mCi/mmol) showed ^{14}C -EDTA and ^{65}Zn appearing in the same fractions (Fig. 3). Fractions that contained the ^{65}Zn and ^{14}C -EDTA had similar retention characteristics on gel filtration as those containing the ^{65}Zn in the first group of chickens and the ^{65}Zn and ^{14}C -histidine in the second group. Ratios obtained for ^{14}C -EDTA to ^{65}Zn (Table 1) revealed no exchange of either ^{14}C -EDTA or ^{65}Zn during passage from the intestinal lumen to the blood plasma, as previously reported⁵. This lack of exchange indicates that the ^{14}C -EDTA- ^{65}Zn complex in the intestinal digesta was transferred intact to the intestinal mucosal proteins and then to the blood plasma proteins.

Chickens fed 1% aspirin in the diet were dosed with 50 μCi of ^{65}Zn and 3×10^{-4} mM ^{14}C -aspirin (specific activity 0.9 mCi/mmol). The fractions from gel filtration were counted for ^{65}Zn and ^{14}C -aspirin and total zinc content was determined by atomic absorption spectrophotometry. Aspirin caused no alteration in the normal elution pattern of intestinal digesta or mucosal soluble fraction (Fig. 4*a* and *b*). In both cases ^{14}C -aspirin and ^{65}Zn were eluted in the same fraction, indicating binding between zinc and aspirin. Aspirin was bound to the same protein in the mucosal soluble fraction (Fig. 4*b*) that carried zinc (Fig. 1*b*). No alterations in the ratios ^{14}C -aspirin to ^{65}Zn in the intestinal digesta or mucosa (Table 1) occurred, suggesting that an aspirin-zinc complex from the intestine binds to a protein in the mucosa. Blood plasma showed alterations from the normal elution pattern of plasma (Fig. 5*a*, *b* and *c*). Graphs obtained for the elution of samples from all three birds are shown. After aspirin treatment alterations in the elution pattern obtained by reading absorbance at 290 nm

could be caused by changes in plasma proteins or by the aspirin fed in the diet, since aspirin has a maximum absorption at 310 nm⁸ and may bind to proteins⁹. Absorption by protein at 280 nm is due chiefly to aromatic ring structure in some amino-acids, therefore small amounts of aspirin bound to proteins may cause large increases in absorption at this wavelength. ¹⁴C-aspirin, however, was not present in all peaks obtained, supporting the idea that plasma proteins have been altered.

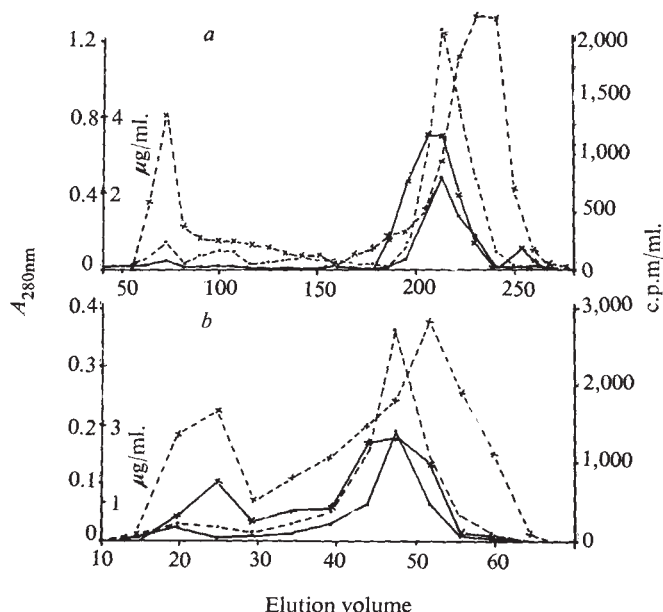


Fig. 4 'Sephadex' gel filtration of samples from three birds dosed orally with ⁶⁵Zn and ¹⁴C-aspirin. Graph was obtained from one bird representative of the three. *a*, Intestinal mucosa soluble fraction elution by 'Sephadex G-150' columns. *b*, Intestinal digesta preparation elution by a system of 'Sephadex G-50' and 'Sephadex G-10' columns. $\times$ --- $\times$, Absorbance; $\bullet$ — $\bullet$, ⁶⁵Zn; $\bullet$ --- $\bullet$, ¹⁴C-aspirin.

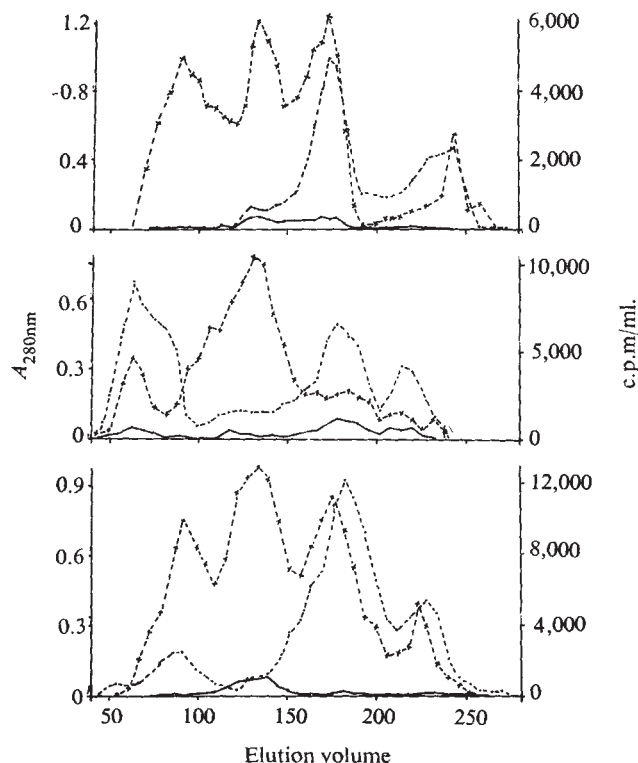


Fig. 5 'Sephadex' gel filtration of blood plasma samples from three different birds dosed orally with ⁶⁵Zn and ¹⁴C-aspirin. Each graph was obtained from a different chicken in the group. $\times$ --- $\times$, Absorbance; $\bullet$ — $\bullet$, ⁶⁵Zn; $\bullet$ --- $\bullet$, ¹⁴C-aspirin.

Data from all three chickens show less ⁶⁵Zn activity in blood plasma. Large increases in the ¹⁴C-aspirin: ⁶⁵Zn ratios in plasma (Table 1) compared with intestinal digesta and intestinal mucosa indicate that ¹⁴C-aspirin-⁶⁵Zn complex was broken and the ⁶⁵Zn transferred.

Following oral administration of aspirin, the levels in plasma decrease sharply¹⁰ after a rapid initial rise, while the levels of salicylic acid increase due to hydrolysis of the ester. Thus, ¹⁴C-aspirin labelled at the carbonyl group of the salicylate ($\text{CH}_3\text{-COO-}(\text{C}_6\text{H}_4)\text{-(}^{14}\text{COOH)}$) was partially hydrolysed 2 h after dosing, leaving ¹⁴C-aspirin and ¹⁴C-salicylic acid in the plasma. This breakdown could be responsible for the loss of ⁶⁵Zn activity observed in the present experiment. Rapid metabolism of aspirin also offers an explanation for the erratic distribution of ¹⁴C-activity in the plasma of the chickens fed aspirin.

These results indicate that zinc is present in the animal body as a metallo-ligand complex. They indicate that zinc is transferred from one protein to another as a metallo-ligand complex. Thus, the possible role of the ligand in these systems is expanded considerably. One could speculate that the metal may be transferred to an enzyme as the metallo-ligand complex and the ligand may have a major influence on the activity of the enzyme.

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Inhibition by Arousal of Epilepsy Induced by Chlorambucil in Rats

In clinical and experimental epilepsy, transient fluctuations in susceptibility to seizures have been shown to result from changes in behavioural state. For example, spontaneous electroencephalographic (EEG) and overt behavioural signs of seizures have been reported more frequently during periods of relaxation or sleep than during periods of alertness or arousal in epileptic patients^{1,2}. Furthermore, sensory stimuli that produce alerting and orienting responses also interrupt seizure activity in patients³⁻⁵ and in animals with various types of experimental epilepsy⁶⁻¹¹. In addition, seizures produced in cats by subcortical application of aluminum oxide¹² or systemic injection of metrazol¹³ have been interrupted by electrical stimulation of the mesencephalic reticular formation, a neural network believed to underlie behavioural and EEG arousal¹⁴.

Although such results suggest a general inverse relationship between seizure susceptibility and arousal level, their clinical significance is unclear because of symptomatic differences

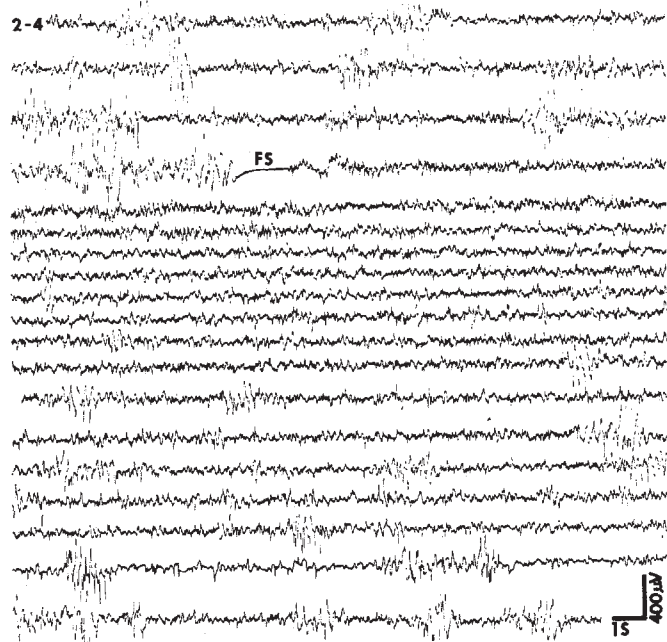


Fig. 1 Foot shock-produced blockage of epileptiform activity in a "nonfocal" subject. Recordings are continuous and each line contains approximately 20 s of activity.

between clinical epilepsy and experimental seizures. Furthermore, those investigators recognizing that sensory stimulation could interrupt ongoing epileptiform discharges have neglected the question of whether an arousing stimulus could produce a relatively long period of decreased susceptibility to seizures by inhibiting seizures that would normally have developed after stimulation.

In rabbits and cats¹⁵ as well as monkeys¹⁶ systemic injections of the nitrogen mustard derivative chlorambucil (*p*-(N-dichlorethyl) amino-phenylbutyric acid) produce behavioural and EEG effects symptomatically akin to those seen in human *petit mal* epilepsy. For example, in the monkey momentary lapses of attention, resembling the "absence" of *petit mal*, tend to occur in conjunction with EEG spike-and-wave discharges similar to those seen in epileptic patients¹⁶. We have traced the development of epileptiform activity due to chronic chlorambucil treatment in the rat and determined the degree to which this activity can be influenced by arousing sensory stimulation. To determine the generality of our results, we also studied the effects of sensory stimulation upon seizure activity in rats with epileptic foci produced by cortical application of ethyl chloride.

Monopolar, stainless steel, extradural electrodes for recording the electrocorticogram (ECoG) were implanted in the skulls of eight, male, hooded rats (200–350 g) under combined pentobarbital (30 mg kg⁻¹) and chloral hydrate (125 mg kg⁻¹) anaesthesia. The materials and methods used have been described before¹⁷. Electrodes referred to as 1 and 2 were placed at bilaterally symmetrical points over the left and right hemispheres, respectively, 2 mm lateral to the sagittal suture and 1 mm posterior to bregma. Electrodes 3 and 4 were located over the left and right hemispheres, respectively, at points 2 mm lateral and 1 mm anterior to the intersection of the lambdoidal and sagittal sutures. In the cases of four of the rats (focal animals), the surgical procedures included production of a 2 mm diameter trephine hole at a point just anterior to electrode 2. The underlying dura was incised and retracted

and a fine spray of ethyl chloride was directed onto the exposed pial surface. After cortical swelling had subsided, the bone disk removed during trephination was replaced.

After surgery, animals were housed individually in 'Plexi-glas' cages fitted with stainless steel grid floors and were allowed continuous free access to food (Purina rat chow) and fresh water. ECoG and motor activity were recorded on each of the first 11 postoperative days. Beginning 5 days after surgery, each animal received an intraperitoneal injection of chlorambucil (12 mg kg⁻¹) each day for 5 days after each day's recording session. The effects of foot shock and other sensory stimuli were studied only on the final day. Methods used for controlling the delivery and timing of foot shock and to prevent both amplifier blocking and inadvertent short circuits through the neuraxis during foot shock have been described before¹⁷.

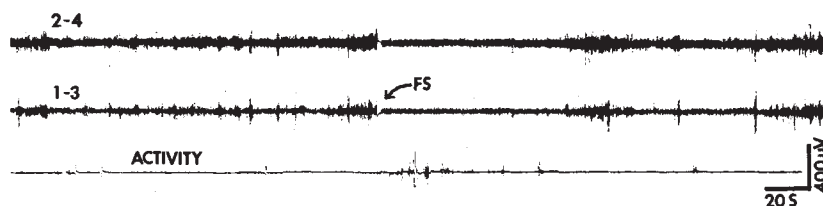
An increase in the overall amplitude of the ECoG was the first observable effect of the epileptogenic treatments and was seen on all channels after one or two chlorambucil injections in the nonfocal (chlorambucil only) animals. In the animals with ethyl-chloride lesions, the increased amplitude developed before chlorambucil injections and was initially restricted to the area around the focus. In both groups, this increase in ECoG amplitude was accompanied by the appearance of epileptiform spikes. With subsequent injections the frequency of spiking increased and bursts of spike-and-wave-like patterns began to punctuate the records of all animals. These bursts, invariably bilateral and synchronous in the nonfocal animals, were only occasionally unilateral in the focal animals. But spike-and-wave patterns occurring in cortical areas some distance from the focus were usually of smaller amplitude than those arising from near the focus, and development of focal epileptiform activity often preceded discharges in other cortical areas.

The spike-and-wave bursts, like those previously reported after chronic administration of chlorambucil in the monkey¹⁶, were similar to the classical spike-and-wave discharges seen in *petit mal* epilepsy or after acute injection of chlorambucil^{15,16} except that the frequency of discharge varied between 3 and 7 s⁻¹, almost twice the usual rate of *petit mal* discharge. These bursts lasted up to 3 s but often consisted only of a single spike and wave. Bursts of spikes and high-amplitude sharp wave also were common.

Epileptiform discharges seemed to be inversely related to the activity level of the subjects. Epileptiform activities rarely occurred during gross bodily movements such as eating, grooming or walking, but were usually seen during periods when the animals were completely relaxed or making slight intermittent body movements (Fig. 1). All motor activity stopped before the onset of epileptiform activity and did not recommence until the ECoG had returned to normal except in a few animals in which head twitches occasionally accompanied spikes. Both the cessation of bodily movement and spike-related twitches commonly accompany *petit mal* spike-and-wave discharges¹⁸.

By the eleventh postoperative day (the day after the fifth and final injection) all animals had reached a consistently high rate of epileptiform discharge. At this time the effects of arousing stimuli on epileptiform activity were examined. Noises, lights, odours, and foot shock were used. In all cases stimulation led to ECoG desynchronization and in many cases to behavioural activation. The most striking effect of stimulation, however, was the interruption of ongoing seizure activity and the production of a relatively long seizure-free period. Examples of the blockage of nonfocal and focal ECoG

Fig. 2 Foot shock-produced blockage of epileptiform activity in a "focal" subject. Notice the higher amplitude of the upper trace (electrodes 2 and 4) which resulted from the ethyl chloride lesion near electrode 2, and the inverse relationship between epileptiform and behavioural activity.



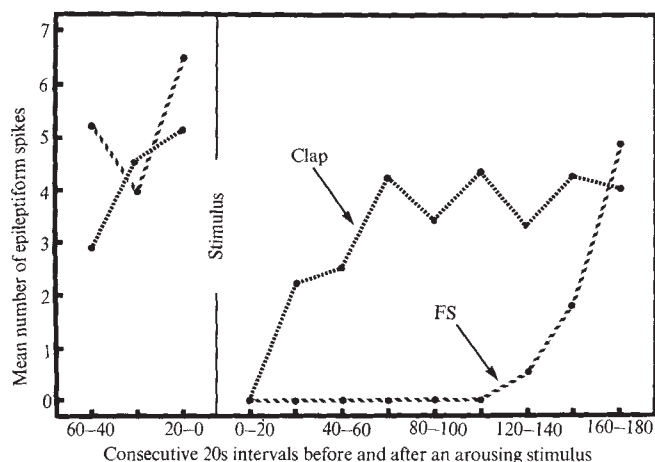


Fig. 3 Mean spike discharge before and after the administration of an arousing stimulus in the "nonfocal" subjects. Counted as spikes were all electrographic waves with amplitude $> 200 \mu\text{V}$ and duration $< 50 \text{ ms}$. The arousing stimuli were a handclap or a 0.4-mA, 0.1 s foot shock.

seizure discharges are shown in Figs. 1 and 2 respectively. In each case a mild FS (0.1 s, 0.4 mA, a.c.) was administered during a period marked by a high incidence of epileptiform discharge. The result was a complete and relatively prolonged inhibition of epileptiform ECoG activity in the period after stimulation. Mildly arousing stimuli such as a handclap or light flash generally produced inhibition of epileptiform discharges lasting up to 1 min. Stimuli such as mild foot shock produced inhibition lasting from 1–3 min. The most striking examples of blockage were seen when painful foot shock was used. A 1 s, 3 mA, a.c. foot shock was found to inhibit epileptiform discharge for 20 min in an animal whose ECoG exhibited four or five spike and wave bursts per minute in the prestimulus period. This relation between the "intensity" of the arousing stimulation and the duration of the ensuing decrease in seizure susceptibility is shown in Fig. 3.

These results extend clinical and experimental reports of antagonism between high levels of arousal and seizure activity. We believe that it may become possible to exploit this for therapeutic purposes. Work in progress in our respective laboratories has helped us by-pass two obstacles which might limit the effectiveness of such a technique. One is that, once a seizure discharge is under way, an arousing stimulus may shorten but not prevent its occurrence. The second is that many varieties of seizure discharge (*petit mal* not included) are accompanied by a loss of responsiveness to sensory stimulation. Our finding that arousing stimuli can not only interrupt ongoing seizure activity but can suppress discharges which otherwise would have occurred in the post-stimulation period and our earlier (independent) observations that the behavioural¹¹ and ECoG¹⁷ consequences of an electroconvulsive shock can be inhibited by antecedent exposure to arousing stimuli suggest that these obstacles can be by-passed. If sensitive methods can be developed for anticipating the onset of seizures, it may prove possible to reduce the frequency and/or severity of seizures in a controlled and relatively nontraumatic way.

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Decomposition of Methylazoxymethanol, the Aglycone of Cycasin, in D₂O

CYCASIN, the toxic principle found in the nuts, roots, and leaves of *Cycas circinalis* L. and *Cycas revoluta*, is carcinogenic to rodents and has hepatotoxic, neurotoxic, teratogenic and radiomimetic properties^{1,2}. Convincing evidence has accumulated that the activity of cycasin, a β -glucoside of methylazoxymethanol (MAM), is due to the aglycone released by the action of β -glucosidases which are present in the plant or produced by the intestinal microflora of the test animal. Thus, MAM is toxic to rats when administered either by the parenteral or intraperitoneal route, while cycasin is toxic only when given orally³. Moreover, cycasin given orally to germ-free rats is well tolerated and is nearly quantitatively excreted unchanged, whereas the same treatment to conventional animals results in death⁴.

The principal end products of the decomposition of MAM in biological fluids are formaldehyde, methanol and N₂. Because metabolic breakdown of cycasin, MAM-acetate or MAM results in methylation of RNA and DNA *in vitro*⁵ or *in vivo*⁶, the formation of a highly reactive methylating intermediate, either diazomethane or a methyl carbonium ion, has been postulated^{7,8}. We present spectroscopic evidence that diazomethane is not an intermediate in the decomposition of MAM in aqueous solutions. This was provided by analysis of the proton magnetic resonance spectra of the products of the decomposition of MAM in D₂O. C–D bond formation, as would be expected from the solvolysis of diazomethane in this medium, was not observed.

The pure aglycone was prepared by enzymatic hydrolysis of cycasin using a β -glucosidase from almond emulsion followed by repeated vacuum distillation³. It is unstable at room temperature and gives rise to visible evolution of N₂ but can be and has been stored in the frozen state in a sealed glass ampoule at -5°C for more than a year with very little change. Its p.m.r. spectrum in D₂O (Fig. 1a) exhibited a 3-proton methyl triplet at δ 4.14 p.p.m. ($J=1.5 \text{ Hz}$) downfield from sodium 2,2-dimethyl-2-silapentane-5-sulphonate (DSS) and a 2-proton quartet due to the $-\text{CH}_2-$ of the hydroxymethyl group centred at δ 4.98 p.p.m. ($J=1.5 \text{ Hz}$). Some decomposition of the sample before analysis resulting from storage moisture and/or handling at room temperature was evident from the presence of the CH₃OD singlet at δ 3.37 p.p.m. and the methylene singlet due to CH₂(OD)₂ at δ 4.84 p.p.m. This amounted to approximately 10.4%. After 12 h at 37°C , nearly 42%

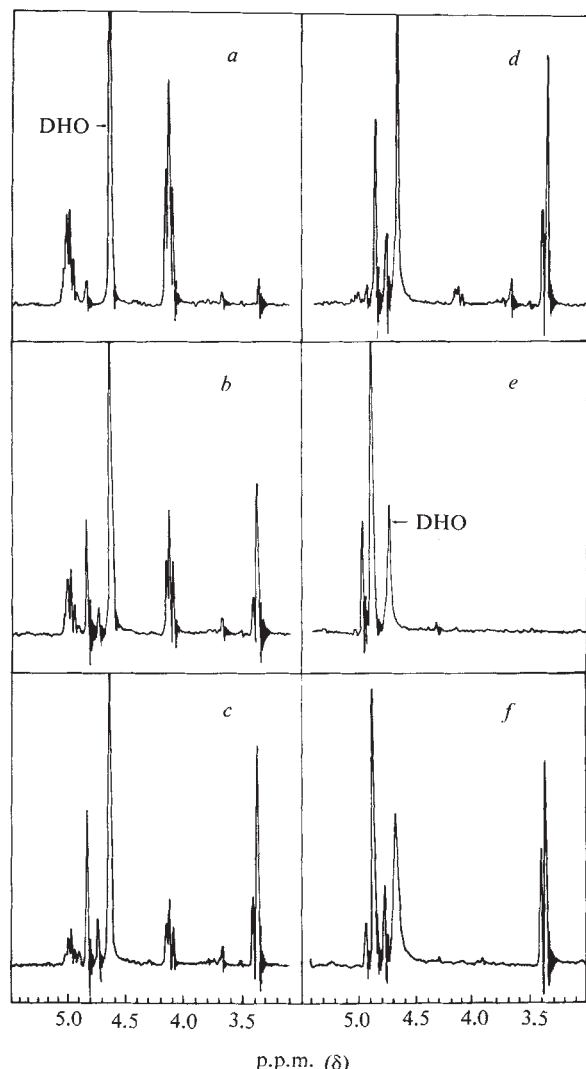


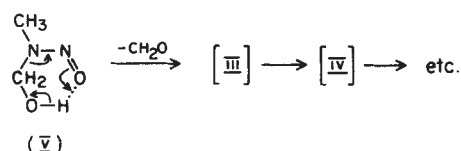
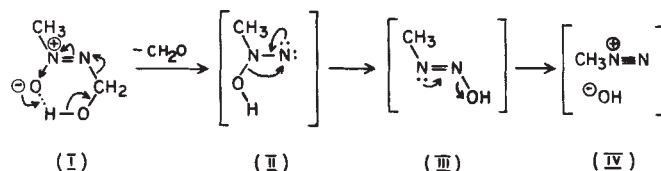
Fig. 1 The decomposition of MAM in D_2O at $37^\circ C$. *a*, Proton magnetic resonance spectrum of MAM in D_2O with DSS internal standard; elapsed time, 10 min; concentration (corrected): 1.58 M; *b*, after 12 h; *c*, after 24 h; *d*, after 48 h; *e*, spectrum of D_2O extract of polyoxymethylene; *f*, same as *e* except CH_3OH added and equilibrated for 3 h. (Varian A-60D spectrometer.)

of the MAM had decomposed (Fig. 1*b*), and after 48 h only 15.5% of the aglycone remained intact (Fig. 1*d*). The decomposition followed first order kinetics with an observed $t_{1/2}$ of 18.6 h.

The end products of MAM decomposition are readily identifiable by reference to Figs. 1*e* and 1*f* which represent, respectively, the spectra in D_2O of formaldehyde and a mixture of formaldehyde and methanol. It is clear that the pair of singlets at δ 3.40 p.p.m. and δ 4.74 p.p.m. (ratio: 1.58) which are slightly downfield and upfield, respectively, from the CH_3OD and $CH_2(OD)_2$ peaks is due to the hemiacetal, $CH_2(OCH_3)(OD)$. This hemiacetal can be detected in the 12 h spectrum (Fig. 1*b*), and its concentration is significant after 48 h. The singlet at δ 4.91 p.p.m. which is observed in Fig. 1*b*, *c*, *d* and *f* represents the water soluble symmetrical trioxane, $(CH_2O)_3$.

The simple first order spectra exhibited by these decomposition products of MAM indicate absence of any exchange reactions of C-H with D_2O . The observed ratios of nearly 3/2 for the methyl/methylene peaks, whether taken totally or individually as their respective components [$CH_3OD/CH_2(OD)_2 + (CH_2O)_3$, and CH_3/CH_2 in $CH_2(OCH_3)(OD)$], constituted further evidence that deuterium was absent in the end-products of the decomposition. In the light of the present observation, a diazomethane intermediate postulated as the active methylating agent arising from MAM decomposi-

tion appears untenable. Such an intermediate should yield CH_2DOD on solvolysis in D_2O , and this would have been readily detected as a triplet of equal intensity with geminal coupling of $J_{H,D} = 2.22$ Hz (ref. 9). The transient methyl donor may in fact be methyl diazonium hydroxide (IV) as proposed by Druckrey¹⁰. This can arise either directly from MAM or indirectly from the cyclic intermediate (I) through the azene (II) and the diazohydroxide (III).



It can be inferred from these results that a d_5 -substituted MAM (or MAM-methyl- d_3) would methylate proteins or nucleic acids with the deuterium atoms intact, quite analogously to the situation obtained with dimethylnitrosamine- d_6 , as observed by Lijinsky *et al.*¹¹. Such experiments are now in progress. The spontaneous decomposition of methyl(hydroxymethyl)nitrosamine (V) formed by enzymatic hydroxylation of dimethylnitrosamine¹² probably follows a formally similar course. The identity of these mechanisms may explain the similarities of the biochemical actions of MAM and dimethylnitrosamine⁶.

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Biochemical Specification versus Specific Regrowth in the Innervation of Skin Grafts in Anurans

FROM studies of the reflex responses of the adult animal¹⁻⁴, it seems that specification of cutaneous nerves in the anuran

tadpole depends on the type of skin innervated. In the frog, *Rana pipiens*, in which specification does not seem to occur much before the onset of metamorphosis, rotation of large patches of back and belly skin through 180° early in larval development results in the development of white belly skin on the frog's back and dark skin on its belly. If the rotation operations are carried out early enough in larval development, the adult wiping reflex responses seem to be permanently misdirected: stimulation of the belly skin grafts results in wiping reflexes directed towards the animal's belly, whereas stimuli applied to the grafted back skin result in a reflex movement directed towards the animal's back. Tadpoles operated on in such a manner after larval stage XV⁵, however develop only normal reflex behaviour^{2,3}. Allowing 6–12 days regeneration time (R. E. B., unpublished), specification must occur at the onset of metamorphosis: stages XVIII–XXI. Local cutaneous nerves grow into the nearest available skin^{2–4,6} which has led to the suggestion that the maladaptive reflex behaviour results from central readjustment of synapses according to specification from the peripheral skin.

The experiments reported here were designed to test the alternative hypothesis of specific regrowth of nerves to the sites at which they originally terminated⁷. There are three ways in which this might occur. (1) Nerves cut during the transplantation operation regenerate towards the periphery but, instead of making functional connexions with inappropriate end-organs, continue "searching" for their original innervation sites until these have been found and functional connexions re-established. (2) Cutaneous nerves regenerate and make temporary, functional connexions with the skin grafts; but at a crucial period of development, for example metamorphosis, these connexions are broken with accompanying axonal degeneration to the perikarya. A new axon then grows, directed towards the periphery and the original innervation sites, regardless of their location on the body. (3) Cutaneous nerves are capable of making temporary functional connexions with skin grafts, but at metamorphosis come to "realize" their innervation sites are atypical. These neurones then die and are replaced by "spare" dorsal root ganglion cells which form central-peripheral connexions that result in the development of reversed reflexes in accordance with the nature of the reversed skin⁷.

A previous investigation showed that it was possible to produce frogs with greatly reduced areas of back or belly skin through simple autografting transplantations⁴. In this investigation, two types of operations were performed on sixty-seven tadpoles of *Bufo* spp. (corresponding to Taylor-Kollros stages V through XVIII) and fourteen tadpoles of *Rana pipiens* (stages VII through XII). In the first, two large patches of skin, comprising most of the back and belly skin areas on the animal's abdomen, were removed. One skin patch was returned to the animal in an atypical location, that is, back skin patches to the belly and belly skin patches to the back. The remaining skin patch was discarded. The second graft type consisted of removing a large girdle of skin from the trunk of the tadpole, cutting away and discarding either back or belly skin and returning the remaining back or belly skin portions to the trunk: belly skin on the back or back skin on the belly. In both instances the large, open wound came to be covered with regenerating epithelia of the type normally found at that site. Through these means, animals with greatly reduced areas of a particular skin type and increased areas of the opposite skin type could be produced.

Fourteen *Bufo* spp. and three *Rana pipiens* tadpoles survived metamorphosis and were tested for the development of maladaptive reflex behaviour by methods described elsewhere³. Maladaptive reflex responses were elicited from areas immediately overlying a reflexogenous zone boundary, either from the outset of testing or within 10 days of the completion of metamorphosis in all skin-grafted animals. Once these areas of maladaptive reflex behaviour had been established they slowly spread until most of the graft elicited a misdirected reflex

response. The spreading phenomenon and description of the responses have been given in detail elsewhere^{2–4}. These maladaptive reflexes have remained throughout the testing periods. No attempts were made to record from the cutaneous nerves and map receptive fields. Reflex responses elicited from the regenerated epithelia on the animal's back or belly were normal from the outset of display during metamorphosis and remained normal and consistent throughout these investigations.

Of the three possible ways specific regrowth might occur, the first and easiest to disprove was that of peripheral regrowth of the nerve to its original innervation site. Electrophysiological recordings from the cutaneous nerves^{2–4,6} have supported earlier anatomical findings¹ that local nerve supplies innervate rotated skin grafts. The current findings with large patch and girdle patch frogs tend to disprove the second specific regrowth concept of axonal degeneration and regeneration to the original skin type. Cutaneous nerves which had formerly innervated back skin (or belly skin in the case of back skin grafts) were confronted with a periphery possessing little or no back skin with which to connect. It therefore became impossible for these nerves to "find" back skin and establish functional connexions. Yet our animals all developed reflex behaviour which was totally consistent with findings on back-to-belly patch rotations on one side of the frog's abdomen with both skin types present^{2–4}. Maladaptive reflex responses developed in all animals examined, either at the outset of testing or shortly thereafter; and the maladaptive reflex behaviour spread over most of the graft surfaces until most of the grafted skin elicited misdirected responses.

The third possibility, of using "spare" neurones to replace degenerating ganglion cells which have innervated grafted skin, has yet to be totally disproven. Cell death is a common phenomenon during development in many animal species^{8–10}, so it is not difficult to conceive of a replacement process which would eliminate the need for peripheral or central readjustments of nerve endings in response to chemical stimuli. But in spite of the attractiveness of the neuronal replacement hypothesis, one must wonder how these "spare" nerve cells can form reflex arcs which will produce maladaptive behaviour without the use of an information exchange with their peripheral contacts. How can cutaneous neurones innervating grafted belly skin for the first time "know" that they must direct their central associations with neurones mediating forelimb wiping reflexes? Rather it seems that such neurones are "informed" of their connexions in the periphery and make central connexions accordingly.

Since transport of axoplasm in nerve cells was first demonstrated¹¹, large numbers of investigations have shown the existence of bidirectional flow of materials in damaged axons¹² and more recent experiments have suggested the presence of a retrograde transport of materials in undisturbed axons^{13–15}. Epidermal products have been shown within cutaneous nerve axons and cell bodies^{16–18}, and peripheral uptake of compounds by nerve^{19–21} demonstrates that peripheral nerves can convey chemical compounds from the periphery to their cell bodies. If specification of cutaneous nerves occurs during metamorphosis and is dependent on skin changes associated with metamorphosis, then any change in the character of the skin must be taken as a possible starting point in a search for information transfer from the skin to the nerve. Investigations are in progress which might demonstrate retrograde transport of skin products to cutaneous nerve cell bodies via their axons. How the nerve reacts to epidermal changes during metamorphosis is unknown.

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Decrease in Chloroplast Content of Barley Leaves infected with Powdery Mildew

POWDERY mildew fungi (the Erysiphales) cause many important plant diseases. These fungi are obligate parasites, as they attack only living host tissue and cannot yet be cultured axenically. They exhibit extreme host specific parasitism and the biochemical mechanisms which determine host resistance or susceptibility are still obscure. Because of their basic metabolic importance, people have sought to determine whether alterations occur in nucleic acids after infection. Millerd and Scott¹ reported that infection of susceptible barley leaves with powdery mildew resulted in increased amounts of RNA in host tissue and four days after inoculation there was approximately 20% more RNA/μg DNA than in non-infected leaves. In contrast, no change was observed in the amount of RNA after inoculation of resistant barley varieties. Malca *et al.*² determined the base composition of RNA in susceptible mildew-infected barley leaves at various stages of disease development. They found a relative increase in guanylic acid and larger amounts of all nucleotides, reflecting the higher RNA content of mildewed leaves. Plumb *et al.*³ also reported a slight increase in RNA in susceptible wheat leaves infected with powdery mildew.

Bennett and Scott⁴ extended these observations by studying changes in chloroplast and cytoplasmic ribosomes of susceptible barley leaves after infection. Five days after inoculation with powdery mildew a 50% decrease was observed in the amount of chloroplast ribosomes and at nine days after inoculation these ribosomes could no longer be detected. On the other hand, there was an increase in the amount of cytoplasmic ribosomes nine days after inoculation which, with respect to the total ribosomal population, more than compensated for the decrease in chloroplast ribosomes. The decrease in chloroplast ribosomes is interesting because it has been shown^{5,6} that infected susceptible leaves have impaired photosynthetic activity and a loss of chlorophyll commencing about three days after inoculation. In contrast, there was no comparable decrease in these parameters in resistant leaves following inoculation⁶.

We now present evidence that there is some loss of chloroplast polysomes in susceptible but not resistant leaves one day after inoculation when the reaction of the host to the pathogen is being determined.

The barley varieties used in this investigation were two near-isogenic lines of the variety Manchuria, designated M1622 (susceptible) and M1623 (Algerian × 4/14 Manchuria, resistant) and Proctor (susceptible) to infection by race B0 of the powdery mildew fungus, *Erysiphe graminis* f. sp. *hordei* Marchal. The fungus was cultivated on the susceptible variety Proctor. Plants were grown in a greenhouse at 22°–26° C and inoculated as previously described⁶, five to seven days after sowing when the primary leaf was about 5 cm high. Plants were harvested 24 h later for extraction of ribosomes.

Fig. 1 shows a typical distribution of monosomes and polysomes isolated from non-infected and infected Proctor barley leaves and fractionated in sucrose gradients. The profiles are very similar except for a slight diminution in the chloroplast dimer fraction in infected leaves. The relative amounts of different RNA species isolated from polysomes of non-infected and infected susceptible barley leaves were determined by electrophoresis (Fig. 2). It is clear that chloroplast RNA is decreased in relation to the amount of cytoplasmic RNA following infection. A comparison is made of the molar ratios of cytoplasmic to chloroplast RNA of the polysome population in both susceptible and resistant leaves (Table 1). The ratios are a reflexion of the relative numbers of ribosomes as there is one molecule of each ribosomal RNA per ribosome⁹. In susceptible varieties (Proctor and M1622), the ratio of cytoplasmic to chloroplast polysomal RNA is increased two to

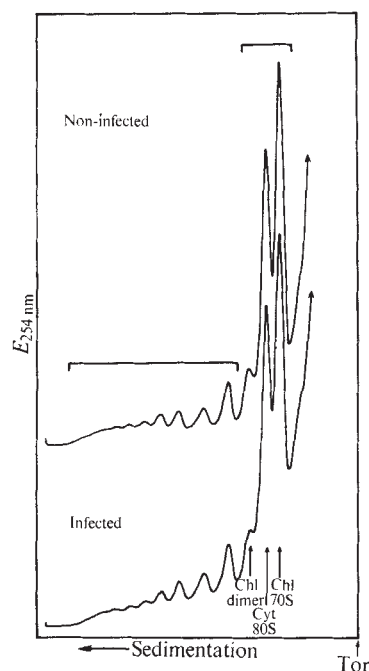


Fig. 1 Ribosome preparations from non-infected and infected Proctor barley leaves. Samples (2 g) were harvested 24 h after inoculation with powdery mildew fungus, and frozen rapidly in liquid nitrogen, powdered and homogenized at 2° C in a 'VirTis' blender containing 10 ml. medium (50 mM Tris-HCl, 50 mM KCl, 10 mM MgCl₂, pH 7.6). The homogenate was made 4% with respect to 'Triton X-100' and strained through one layer of 'Miracloth'. The filtrate was centrifuged at 39,000g for 5 min to remove cell debris and 1 ml. aliquots of the supernatant were placed on discontinuous sucrose gradients. The six layers of the gradients (of volume 6, 5.5, 5, 4, 3, and 2 ml.) consisted of solutions of 34%, 29%, 24%, 19%, 14% and 10% sucrose (w/v) in a buffer containing 50 mM KCl, 10 mM MgCl₂ and 10 mM Tris-HCl, pH 7.6. Gradients were centrifuged at 24,500 r.p.m. for 3 h at 0° C using a Spinco SW 25.1 rotor. After centrifugation, each centrifuge tube was pierced at its base and 50% sucrose was pumped through the aperture. The displaced gradient was monitored by ultraviolet absorbance and the monosome and polysome fractions (indicated by bars) were collected separately. The chloroplast dimers were included with the monosome fraction as they were poorly resolved from the monosomes.

three times 24 h after inoculation (Table 1). In contrast, the same ratio in resistant leaves is only very slightly altered by inoculation. The increased proportion of cytoplasmic RNA could result either from an increase in cytoplasmic polysomes or a decrease in chloroplast polysomes after inoculation of susceptible leaves. As the ratio of polysomes to monosomes is decreased after inoculation (0.45 in non-infected leaves as compared to 0.35 in infected Proctor leaves) this increase in the proportion of cytoplasmic RNA is because there are fewer chloroplast polysomes rather than more cytoplasmic polysomes.

These findings raise two questions: what is their importance in determining resistance and susceptibility, and what are the underlying mechanisms bringing about this observed decrease in chloroplast polysomes in infected susceptible leaves? Development of the powdery mildew fungus during germination, germ tube elongation, appressorial formation and host penetration are similar in susceptible and resistant hosts¹⁰. These processes are accomplished during the first 24 h after inoculation¹⁰. However, the production of elongating secondary hyphae, commencing about 24 h after inoculation, is strongly inhibited in resistant varieties^{10,11}. The observed changes in chloroplast polysomes are, therefore, occurring

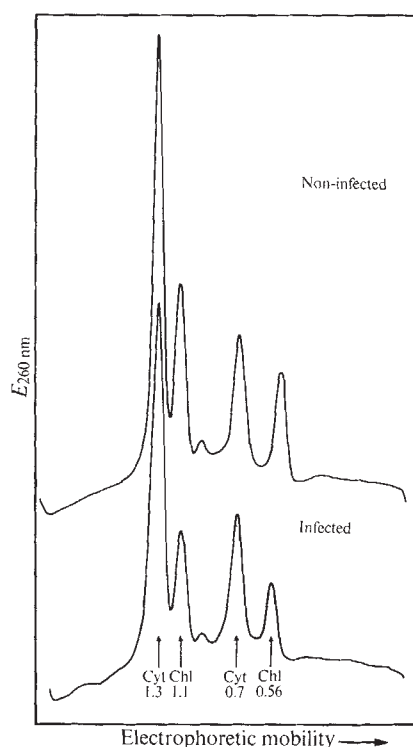


Fig. 2 RNA of polysomes of non-infected and infected M1622 (susceptible) barley leaves. Samples were harvested 24 h after inoculation with powdery mildew fungus and ribosome fractions prepared from them as described in Fig. 1. Ribosomes were precipitated from both monosome and polysome fractions by the addition of 0.7 volume of absolute ethanol (w/v)⁷ and sedimented by centrifuging at 39,000g for 5 min. RNA was dissociated from protein by suspending the pellet in 2.5 ml. sodium dodecyl sulphate/acetate buffer (0.5% SDS, 10 mM MgCl₂, 0.15 M sodium acetate, pH 6.0). The absorbance of this solution was determined at 260 nm to estimate the amount of RNA present. Subsequently 2 volumes of absolute ethanol were added and the mixture allowed to stand overnight at 2° C to allow the RNA to precipitate. After centrifugation, the RNA was resuspended in the electrophoresis buffer (30 mM Tris-HCl, pH 8.1, 0.1 mM EDTA, 0.1% SDS and 2 mM Mg acetate) containing 5% sucrose to give a final concentration of 1 µg RNA/1 µl. buffer. RNA was fractionated in 2.4% polyacrylamide gels at room temperature as described by Loening⁸. Approximately 30 µg RNA was loaded on to each gel and, after electrophoresis, gels were scanned at 260 nm with a 0.2 mm wide light beam using a modified Hilger-Gilford spectrophotometer. The figures below the peaks represent their respective molecular weights in millions.

Table 1 Molar Ratios of Cytoplasmic to Chloroplast RNA of the Polysomes

Plant material	Cytoplasm/chloroplast RNA *
Proctor (susceptible)	
non-infected	1.39
infected	3.07
Manchuria (M1622, susceptible)	
non-infected	1.42
infected	3.43
Manchuria (M1623, resistant)	
non-infected	1.02
infected	1.20

Polysome populations were isolated from susceptible and resistant leaves of barley 1 day after inoculation with the powdery mildew fungus.

* The relative amounts of chloroplast and cytoplasmic ribosomal RNA were calculated from the areas of the 1.30×10^6 molecular weight cytoplasmic and 0.56×10^6 molecular weight chloroplast RNA⁹.

about the same time as events determining resistance or susceptibility and so may be one of the prime factors which affect successful establishment of the pathogen.

Likely explanations for the breakdown of chloroplast polysomes in infected susceptible leaves are one of the following. First, the fungus could interfere with photosynthetic phosphorylation; second, the fungus may inhibit specifically the synthesis of certain chloroplast amino-acids; third, the fungus could produce compounds which specifically interfere with the function of chloroplast 70S ribosomes; or fourth, chloroplast mRNA synthesis and degradation may be altered after infection. As this fungus is an ectoparasite, decreases in chloroplast polysomes could result only from diffusible products of the fungus and the differences noted between resistant and susceptible hosts may reflect different cell and membrane permeabilities to these fungal products in the two host types.

Whatever the cause of the loss of chloroplast polysomes or whether or not the polysomes are the primary site at which resistance or susceptibility is determined, the decrease in their amount undoubtedly affects the functioning of chloroplasts and leads to some of the disease symptoms which are only detectable at later stages of infection than those studied here.

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BOOK REVIEWS

Life from Crystals

The Life Puzzle: On Crystals and Organisms and on the Possibility of a Crystal as an Ancestor. By A. G. Cairns-Smith. Pp. vii + 165. (Oliver and Boyd: Edinburgh, October 1971.) £1.95.

CRYSTALS have featured in earlier speculations on the origin of life as catalysts for the reactions of simple molecules in the "primaevial soup" and their conversion into more complex molecules in the early stages of a primitive biochemistry. This book, in its closing pages, which are the climax of a lively discussion of the organizational aspects of the origin of life on Earth, makes the bold suggestion that inorganic crystals may have played a more sophisticated role, may in fact have been the first genes. The definition of the word "gene", for this thesis, will have to be broad enough to include self-replicating entities of completely different chemical constitution from those which are central in our present biochemistry; and the suggestion implies that there was, in the early stages of biochemical evolution, a major switch (perhaps more than one) of genetic materials.

A bold suggestion indeed; but one that deserves serious consideration. It is not made lightly or without antecedents, but is presented as the outcome of a well-reasoned consideration of the more general aspects of the evolution of organisms: not the chemical evolution of simple molecules towards nucleic acids and proteins, but such things as the extreme improbability of molecules of these types being formed by chance ("Blind Chance is a creative but very limited fellow"), the principles of self-reproducing organisms, and the part played by natural selection in the evolution of molecular species. In short, the author tries to understand why replication and selection, acting on the products of chance, were important, probably essential, factors in the evolution of the complex molecules of our present biochemistry.

The book is written in an extremely lively colloquial style which makes it eminently readable; and the exposition is made the more attractive by many

homely analogies. For example, use is made of the pictorialism of Waddington's "epigenetic landscape": this originally illustrated the development of different kinds of cells in any one organism by a gently sloping plane with branching grooves in it (a landscape contrived by the genes), down which a ball can roll to one of several different places. Cairns-Smith uses a similar model with a mobile landscape to represent the effect of changes of molecular environment on the evolution of an organism. And so to the following delightful picture to symbolize evolution converging to particular species and simultaneously diverging to different species: "Think of a very large blanket covering a dense crowd of randomly browsing tortoises. A handful of peas placed in the middle of the blanket would first settle into a local depression and then probably become scattered into progressively more numerous separate clutches in separate local depressions."

Let it not be supposed that this light-hearted imagery denotes a light-weight approach to serious matters. The approach has all the necessary weight; and the consideration of general underlying principles sometimes leads, not unnaturally, to deeper philosophical levels. A defence of teleological language (often regarded as dangerously unscientific because it may seem to imply purposeful striving towards some future state) contains the following perceptive remark: "Modern science frequently resorts to a non-animistic teleology—even if she usually keeps quiet about it. Curiously, in physical science, it is in that most respectable branch—classical thermodynamics — that teleological thinking is most rife".

The outcome of the consideration of general principles is a list of the requirements which the original genes would have to satisfy; and the favoured candidate, it is suggested, is some sort of crystal. To have sufficient information-carrying capacity, the crystal would have to be of some complexity; replicability could be provided by ready cleavage; and these requirements, together with presumed availability, point to a layer silicate, perhaps a clay mineral. In such crystals, the necessary complexity could

be provided by a pattern of replacements of silicon by aluminium, and this, with the associated pattern of electrical charges, could be the basis for printing of the pattern from one layer to the next. Highly organized associations of simple organic molecules with clay minerals are well known, and thus we have in principle a primitive life-system with crystals as the self-replicating genes which control the synthesis of complex organic substances from simpler ones.

In our present biochemistry, based on nucleic acids and proteins, inorganic crystals are not involved, so the suggested scheme implies that there was a major switch of genetic materials, organic substances replacing inorganic crystals as genes. A take-over of the genetic function by organic substances which were once just links in the chain of reactions is envisaged. (The author again enlivens the discussion, this time by a commercial allegory.)

The idea of a take-over, at first sight so daring, is not so difficult to swallow as might at first appear. Indeed, it acquires plausibility from a close-at-hand parallel. Reactions between simple organic molecules were, in the beginning, almost certainly catalysed by inorganic crystals, possibly clay minerals; but now, in living organisms, such reactions are catalysed by enzyme proteins. There has thus almost certainly been a take-over of the catalytic function by proteins from inorganic crystals, so why should there not have been a take-over of the genetic function by nucleic acid-type substances from inorganic crystals? Possibly the same crystals, or crystals of the same general type, did both jobs at first, but faded out of the picture when the two types of polymeric products were found to be more efficient and more versatile in their specialist fields. Polypeptides found that they could catalyse simple reactions by themselves without help from crystals, and nucleic acid-type molecules found that they could replicate by themselves without help from crystals. This is the broad picture of early biochemical evolution to which Cairns-Smith's ideas lead.

This is a thought-stimulating book, worthy of the attention of all who are

interested in speculations on the beginnings of biochemistry. The ideas, which have been published elsewhere in recent years, are here collected into a coherent account, which will no doubt stimulate attempts to achieve experimentally the sort of crystal-controlled biochemistry envisaged in these bold speculations.

C. W. BUNN

Environment

Man and the Ecosphere. By Paul R. Ehrlich, John P. Holdren and Richard P. Holm. Pp. viii+307. (Freeman: San Francisco and Reading, September 1971.) £5.20 cloth; £2.50 paper.

Man's Impact on the Global Environment: Assessment and Recommendations for Action. (Report of the Study of Critical Environmental Problems. Sponsored by the Massachusetts Institute of Technology.) Pp. xxiii+319. (MIT: Cambridge, Massachusetts, and London, January 1971.) £5.85 boards; £1.40 paper.

The Ecological Context. By John McHale. Pp. 188. (Studio Vista: London, March 1971.) £3.15.

Books on environmental subjects are so numerous that they pose a threat, not so much to the trees that provide the paper, but to the credibility of "environmentalists". Doommongering, from being an occupational hazard of ecologists, has reached epidemic levels. The result is that legitimate concerns about the maintenance of some degree of environmental quality are in danger of being ignored because of the exaggerated or at least unproven assertions which receive so much publicity. Fortunately, none of the three books listed above falls into the eco-fanatic class and two of them are worthwhile additions to overcrowded bookshelves.

Man and the Ecosphere is best described as a useful piece of recycling with editorial comments that make it even more valuable. It is a collection of twenty-seven articles from the *Scientific American* selected by the editors to present "... a variety of aspects of the growing crisis in population, resources and environment ...". The articles are classified under four headings: "The ecosphere and pre-industrial man"; "Limits rarely perceived"; "The dimensions of intervention" and "On management and buying time". The original dates of publication range from Iverson's paper, on "Forest Clearance in the Stone Age", published in 1956 to Gough and Eastland's "Prospect of Fusion Power" which first appeared in 1971.

The articles are an excellent sample of some of the best writings to appear in the *Scientific American*. They have been skilfully selected and the editorial

introductions to the four sections provide controversial, up to date assessments of many of the papers. The subjects covered include food production, the human population, water, toxic substances, pollution, the carbon dioxide problem, ionizing radiation, an assessment of technology, chemical fertilizers, third generation insecticides, and urbanization. The editors' conclusions are sometimes in opposition to those of the authors and they do not hide the fact that they are impatient with optimistic or "balanced" viewpoints. Edward Deevey Junior is taken to task for including the ideas of Arnold Harburger and Colin Clark in his contribution on "The Human Population". The high quality of Braidwood's account of "The Agricultural Revolution", whilst fully appreciated by the editors, earns the comment that this major step in cultural evolution "... might reasonably be called a journey towards oblivion".

Popular science of the *Scientific American* type, though invariably well written and well illustrated by recognized authorities, can sometimes be bland. The controversial attitudes of the editors give many of the papers new meaning and they present the reader with an intellectual challenge which makes the volume one of the best general introductions to many of today's problems.

Man's Impact on the Global Environment is a study of critical environmental problems (SCEP) undertaken as a contribution to the UN 1972 Conference on the Human Environment. It concentrates on the effects of a selected group of pollutants at the global level. The writers do not underestimate the importance of local and regional studies but their approach underlines the "space-ship" concept of Earth and the universal nature of pollution problems. It is a book which should be read, not only for its assessment of some major aspects of pollution and its recommendations for action, but as a case-study of how intensive, short-period, collaborative investigations on matters of immediate concern should be planned.

The Steering Committee under the chairmanship of Dr Carroll L. Wilson (Professor of Management at the Massachusetts Institute of Technology) first met in the autumn of 1969. The detailed working sessions in July 1970 were attended by some forty US specialists and another thirty persons contributed on a part-time basis. The finer points of editing were sacrificed for speed of publication and the report appeared in 1970.

This study of the effects of pollutants on the "atmosphere-land-ocean" system is refreshing for the care which is taken to separate fact from conjecture and for its atmosphere of scientific detachment touched with a sense of urgency.

The report of the working group on climate includes surveys on the carbon dioxide problems, the presence of particulate matter in the atmosphere, and the influence of sub-sonic and super-sonic aircraft. The ecological effects group gave special attention to DDT, mercury, oil and phosphates as pollutant types. The group on monitoring describes the types of information that must be collected if we are to have an adequate basis for assessing methods of control and degrees of environmental damage. It is unfortunate that the section on monitoring the effects of SSTs was not available before they embarked upon the production of such types of aircraft.

The working group on implications for change concentrated on the economic, social and political aspects of pollution problems. Its conclusions should certainly be read by those ecologists and environmental scientists who believe that they have all the answers. In describing the political process it points out that "... it is wary of positive assertions that turn out to be unfounded and of experts who do not distinguish between their allegations within the field of their expertise and their allegations made as citizens commenting upon general matters".

The publisher's blurb describing *The Ecological Context* tells us among other things that "The author has written a significant document for use in humanizing this world for man's use through the physical energy and materials systems at our disposal." Perhaps those in search of the key to "humanizing" (whatever that means in this context) may find a clue in this book. The author's preface makes it clear that the book is not "... definitive in the area of ecology ..." and after defining applied human ecology as "planetary housekeeping" the scene is set for a bewildering assortment of ideas and facts. Naturally, when the word "ecological" is given prominence in the title, I have looked for accuracy in the book's ecological content. In a brief reference to DDT we learn that "... the 'threat to survival' of higher organisms was first noticed through its accumulation in the tissues of penguins in Antarctica". This statement ignores the outcry which followed the publication of *Silent Spring* in 1962, and which predated the first publication on DDT content of Antarctic penguins by some years. A few pages further on, we are left to draw our own conclusions from the statement that "... it has been calculated that certain elements, for example argon, neon, krypton, and so forth, essential to life maintenance are now being 'mined' out of the atmosphere by industrial operations at a faster rate than they are being produced by natural processes".

The Ecological Context has an abundance of charts packed with information. Their contents are perhaps justified within the catholicity of "planetary housekeeping". In addition to prosaic down-to-earth charts of biogeochemical cycles, we are given insights into such things as "Man's increasing vertical mobility", and "Man's increase of knowledge: Time, space, energy, and electromagnetic spectrum". There is a chart on "The progress of computer technique" which depicts the number of computers installed in various countries up to 1965. It is fortunate that the sources of the charts are given because the book is without an index and the reader who turns to it for information will have to do his own searching.

Like so many "significant documents" on environmental subjects, the book disturbs me. Ecology as a discipline has a structure but many of its basic concepts lack the solid, factual and predictive content that are the necessary foundations for its progress as a science and as ground rules for the management of renewable resources. Too much should not be written into, or out of, the still far from complete structure of ecology. Perhaps I take too pessimistic a view of the dangers which beset ecology now that it has entered the public domain. If I do, it is because I believe that whilst it has many lessons for those concerned with environmental management, those who dispense it should not disguise its limitations.

Man's Impact on the Global Environment makes it very clear that we cannot rely on many of the data now available to us. In commenting on them they say: "In the process of making judgements we found that critically needed data were fragmentary, contradictory, and in some cases completely unavailable. This was true for all types of data—scientific, technical, economic, industrial and social." Plans are now being drawn up to ensure that some time in the future we shall have more reliable data. Several international organizations and committees are now giving consideration to the establishment of a global network for monitoring the environment. ICSU through its Special Committee on Problems of the Environment (SCOPE) has produced a monitoring programme which incorporates many of the proposals made by SCEP. The International Biological Programme (IBP) is approaching its final stages and its studies on biological production, although patchy in their coverage of the principal biomes of the world, form a sound basis for the development of certain aspects of monitoring and for the extension of research on the biosphere. The UNESCO programme *Man and the Biosphere* (MAB) which becomes operational in 1972 will, it is hoped, draw heavily on the achievements of

IBP. As yet, the mechanisms for the integration of these and other international efforts are inadequate. Furthermore they neglect important aspects of the man-environment system. The management of the world's resources, the development of solutions to the different population problems, the development of the physical, mental and social needs of the animal *Homo sapiens*, require more than a knowledge of the environment and the effects of pollutants; they demand major changes in the way of life of the species.

Have we the time or the sense of purpose to reach reasonable compromises on a global scale? The UN 1972 Conference on the Human Environment may represent mankind's last chance to provide a fully integrated approach towards the prevention of catastrophe. I hope that those who represent governments at Stockholm will do more than glance at *Man and the Ecosphere* and will certainly read the first thirty-six pages of *Man's Impact on the Global Environment*.

J. B. CRAGG

Amateur Astronomy

Guide to the Planets. By Patrick Moore. Pp. 224+16 plates. (Lutterworth: London, October 1971.) £2.50.

THIS is a new, considerably revised version of a book the last edition of which appeared nearly ten years ago. Much astronomical progress has been made during the interim, and Mr Moore presents this new material, as well as the old, in a very readable way. The result is a book well suited to the amateur astronomer, or keen sixth-former, who seems to be in the author's mind. The considerable number of clearly drawn diagrams are a valuable adjunct to the text, and are of particular value in providing a feel for the relative sizes of objects and of orbits in the solar system.

Mr Moore tends to be rather dogmatic in some of his statements. "Telstar," he informs us, "is still in orbit, though its power has long since failed . . . we could never find it again even if there were any point in looking for it." But there is much to be said for reducing qualifying remarks in an introductory text to the minimum compatible with reasonable accuracy. In fact, very little of the information can be faulted, and the few errors that do occur are mainly trivial. One exception is the assertion that " . . . the inner [Van Allen belt] is made up chiefly of protons, while the outer consists mainly of electrons". A sixth-former who had learnt something of electrostatic forces between similarly charged particles might pardonably feel confused. Some explanation should there-

fore have been given in terms of the particle energies.

The book's chief strength is at the same time its main limitation—namely, its emphasis on amateur interest in the planets. The strength of this approach is evident: Mr Moore can surely claim to have authoritative knowledge of the interests of amateur astronomers. (I suspect, however, that there is an element of mythology in his constant emphasis on the historical importance of amateur studies of the planets during the present century.) But there are many fascinating problems concerning the planets that are not directly related to an amateur astronomer's observations, yet which would certainly enrich his interests. We might, for example, have been told something of commensurabilities between planetary, and satellite, orbits. This is a current area of debate amongst professional astronomers. Again, the most disappointing part of the book is that devoted to the origin of the planets. The great amount of recent, relevant research in this area is largely ignored.

This sometimes excessive emphasis on the amateur approach also appears in the short reading list at the end of the book, for it consists almost entirely of works written by amateurs. Various recent publications, especially some from the United States, have been written by professionals, yet would be of considerable potential value to amateurs. Nevertheless, this is a generally excellent text at the introductory level.

A. J. MEADOWS

Magnetism

Structure and Properties of Magnetic Materials. By D. J. Craik. (Applied Physics Series.) Pp. 244. (Pion: London, 1971.) n.p.

THIS book is the first in a series of textbooks on applied physics, the editor of the series being Professor H. J. Goldsmid. In it the author sets out to provide the groundwork required for an understanding of the behaviour and properties of modern magnetic materials. It begins with a discussion of magnetostatics at the level required for an understanding of magnetic domains and of permanent magnet materials. This is followed by a section somewhat curiously entitled "Magnetic dipoles in applied fields". It deals with the classical (Langevin) theory of paramagnetism, anisotropy fields and magnetic measurements. In the next chapter "Atomic structure" the author makes a valiant though only partially successful attempt to discuss the electronic structure of multi-electron atoms in terms of quantum mechanics and then proceeds to a basically qualitative but rather more successful discussion of

crystal field and exchange effects. Much of this is of direct and special relevance to ferrites and the inclusion of a quite lengthy discussion of Pauli paramagnetism and of Stoner's treatment of itinerant electron ferromagnetism, though it does much to broaden the scope of the book, seems somewhat out of place. The final chapters deal, essentially, with permanent magnets, soft magnetic materials and the theory of ferromagnetic domains. The discussion of domains makes extensive use of the author's own work on magneto-static effects. Bubble domains are not mentioned until the final paragraph. But the relevance of magnetostatic effects to bubble domains is clearly very great and the treatment of domains, at first sight both idiosyncratic and disproportionate, takes on a topical and timely aspect when viewed against the present interest in domain devices.

The book does not seem to be very suitable as a general introduction to magnetism. Topics such as antiferromagnetism, spin-waves and (surprisingly) molecular fields are scarcely mentioned. On the other hand, the author, having selected his field, has wisely refused to stray outside it. One cannot have it both ways. Within its self-imposed limitations this is a useful book.

E. W. LEE

Layman's Cosmology

The Nature of the Universe. By Clive Kilmister. Pp. 216. (Thames and Hudson: London, October 1971.) £2.25.

THE past few years have seen a number of new books on astronomy at the non-technical level. This is a reflexion of the rapid and remarkable development in this field during the past decade, as well as of the layman's curiosity about what goes on "up there". Professor Kilmister's book is intended to provide a stimulus to this curiosity.

The book is divided into eight chapters. The first chapter prepares the reader for the vast distances and long time scales he will encounter in cosmology and acquaints him with some of the objects of interest to the astronomer. The next two chapters are historical, showing how man's understanding of the heavens evolved from the early Greeks to the present century. The author points out the great landmark in this development: the Newtonian laws of motion and gravitation; and makes the important distinction between the descriptive theories which preceded it and the causal ones which followed it. Chapter 4 attempts (not unsuccessfully) to explain the remarkable ideas of special and general relativity. This is followed by a description of the so-called rival theories of cosmology—the big-bang and the steady

state theories. The observational material relevant to these theories, or to the structure of the universe as a whole, is discussed in the next two chapters. Lest the reader should think that there are only two types of cosmological theory, the author devotes the last chapter to a brief survey of other, more esoteric theories which have come from such brilliant minds as Dirac, Eddington and others. Rightly, he leaves the discussion inconclusive, pointing out the pros and cons of the theories, the "ifs" and "buts" of the observations.

The text is easy to read and very well illustrated with diagrams and photographs, some in colour. While the rapid progress in astronomy may make some of the material of this book out of date fairly soon, the book itself should serve as a useful guide to the lay reader for many years.

J. V. NARLIKAR

Hebrew Science

Studies in Hebrew Astronomy and Mathematics. By Solomon Gandz. Pp. xii+544 (Ktav Publishing: New York, February 1970.) \$25.

THE interest of the ancient Hebrews in astronomy and mathematics arose primarily as an incidental consequence of a preoccupation with secular and religious law. A central problem was the establishment of a fixed calendar. In his very helpful introduction to this collection of essays, Professor Shlomo Sternberg of Harvard University summarizes the relevant astronomical observations: the daily rotation of the celestial sphere with the fixed stars; the annual motion of the Sun along the ecliptic as a natural explanation of the disappearance and reappearance of stellar constellations, and of the solstices and equinoxes (the Sun "walks to the south and turns to the north"); the motion of the Moon as a conveniently simple means of keeping track of the days, in spite of the irregular length of the month; and the nineteen-year cycle with seven thirteen-month and twelve twelve-month years (known to the Babylonian astronomers as far back as the fourth century BC).

There seems no reason to doubt the traditional view that the fixed Hebrew calendar was enacted in the fourth century AD, but the absence of a definitive text on the calendar earlier than the eleventh-century *Sefer ha-Ibbur* and the relevant parts of the Maimonides Code has set many problems for students of rabbinic law and its development. Thus in one essay Dr Gandz discusses the argument in the literature as to when eyewitnesses to the appearance of the *hodesh*—the visible new Moon crescent—were dispensed and the new month determined by the

computed *molad* or mean conjunction; in another he enquires at what epoch it became customary to celebrate two new Moon days (compare I Samuel, 20).

The mathematical section includes the original texts with translations of *Mishnat ha-Middot*, a Hebrew geometry from about AD 150, and of a parallel Arabic geometry by al-Khowarizmi. There is an essay on the development of Hebrew numerals and of *gematria*, calculations based on the numerical values of letters, and closer in spirit to cryptography than to mathematics; a rather unconvincing propaganda piece which overcorrects the earlier neglect of Babylonian and Hebrew mathematics and astronomy; and a study of the excursions into mathematics of Saadia Gaon, the father of Jewish scholasticism.

The essay likely to arouse the widest interest is on "The Zodiacal Light in Ancient Hebrew Literature". Dr Gandz claims that this phenomenon—observed and noted in the sixteenth and seventeenth centuries by Kepler, Descartes, Cassini and Hooke—enables us to understand better many references in oriental literature. It is referred to variously by the Arabs as the "false dawn", the "pillar of the dawn", and the "wolf's tail". The ancient Egyptians apparently deified and worshipped this pyramid of light as the "herald and harbinger of the rising sun". (It is even proposed that it accounted for their predilection for building pyramids and obelisks!) Gandz suggests that the author of Genesis similarly had in mind the Zodiacal light when he wrote "Y'hi 'Or"—"Let there be light"—for the work of creation on the first day, deferring the creation of the Sun, Moon and stars until the fourth day. He supports this by a similar translation of the word 'Or in passages from Job, Ecclesiastes and Isaiah. Further, he is convinced that the "pillar of fire" which guided the Israelites out of Egypt by night also refers to the (miraculously magnified) Zodiacal light. In his view, the author of Exodus intends it as an "ironical allusion to the Egyptian god who manifests himself as a pillar of light": Yahweh, the creator of the luminous pyramid (along with everything else), rams home the moral to the Egyptians by employing their "god" to act on behalf of their victims.

Gandz looks forward to the discovery of some analogous meteorological reality behind the "pillar of cloud by day". He is a member of a long line of scholars who have tried to account in naturalistic terms for the phenomena to which the biblical authors allude. His ideas—whether one finds them plausible or fanciful—seem to me to be logically independent of any personal commitment to (or denial of) a theistic world-picture.

L. MESTEL

Nutrition in its Place

Newer Trace Elements in Nutrition. Edited by Walter Mertz and W. E. Cornatzer. Pp. xiii + 438. (Marcel Dekker: New York, November 1971.) \$24.50.

Amino Acid Fortification of Protein Foods. Edited by Nevin S. Schrimshaw and Aaron M. Altschul. (Report of an International Conference held at the Massachusetts Institute of Technology, September 1969). Pp. xxv + 664. (MIT: London and Cambridge, Massachusetts, November 1971.) \$25; £11.65.

Biochemistry of Foods. By N. A. M. Eskin, H. M. Henderson and R. J. Townsend. Pp. vii + 240. (Academic: New York and London, October 1971.) \$12.50; £5.85.

THESE three books illustrate in a particularly vivid way the current debate about the virtues and vices of science. In doing so they bring out, as was inevitable, the attitudes and activities of scientists at their best, that is to say, when they are doing science, and at their worst, when they are laying down the law to princes and principalities, governments, developing nations, even to mankind at large, what "science" tells them should be done.

Newer Trace Elements in Nutrition is a good example of science in its proper sphere. It is a well edited compilation of the papers read at an international symposium held to celebrate the dedication of the Human Nutrition Laboratory in Grand Forks, North Dakota. In his opening chapter, E. J. Underwood, while providing the depth of scholarship and the list of references required in a work of serious science, writes easily and well and makes a number of points worth making. One is that the progress of science so often depends on technique. The Nobel Prize Committee were well advised to make an award to the discoverers of paper chromatography, nor could much be done to fathom the mechanism of diabetes until an accurate method for the analysis of blood glucose had been established. Only since the development of atomic absorption spectrometry and neutron activation has progress been possible in the elucidation of the function of trace elements in nutrition. Another point made by Underwood is that the early studies of the possible nutritional significance of zinc, copper and manganese were done, not to increase agricultural productivity or to cure any known disease, but simply for fun or, as he puts it, from a desire to enlarge knowledge. From this came what the specialists now call "the first golden era" of trace element research leading up to the present when trace metals pro-

vide the same stimulus and excitement that vitamins once had a generation ago.

The introductory chapters, including a businesslike and quite detailed one on the spectral characteristics of trace metals when combined in their biologically active forms as metallo-enzymes, soon move on to the systematic account of each metal in turn. Selenium, as is its due, is given three chapters. The first covers its function as an essential nutrient and its inter-relationship with vitamin E. Then come well documented accounts of the way in which this substance, more toxic than arsenic and credibly reported to be carcinogenic when subjected to the sort of pharmacological tests that throw the US Department of Health and Welfare into fits, may serve as an antagonist — almost an antidote — to arsenic. Knowledge of the metabolic role of selenium is indeed in an interesting, if complicated, state as is borne out by evidence showing that sensitivity to the toxic metabolite dimethyl-selenide is dependent on two factors: exposure to small amounts of mercury and sex.

W. Mertz and E. E. Roginski achieve the considerable literary feat of writing one of the chapters on chromium metabolism, including in it detailed data and graphs and yet producing a result readable and interesting to a non-specialist previously unaware of the part played by chromium in the "glucose tolerance factor" and the interaction between insulin and chromium. The fact that the book as a whole possesses a unity not always achieved by collections of symposium papers can perhaps be attributed to the fact that Mertz together with W. E. Cornatzer edited it. And the contributors have something to say. They have experiments to describe and if from their experimental results they draw conclusions of practical significance—that dietary chromium deficiency may perhaps be concerned with a particular kind of diabetes in children, or with kwashiorkor or certain conditions in postpartum women whose hair may contain sub-normal concentrations of chromium—this is a welcome extra to the primary object of finding something out. Perhaps R. J. Hankin in his paper on zinc metabolism was just a little disappointed at having to describe the decreased taste acuity he observed as "idiopathic hypogeusia".

This leads me to *Amino Acid Fortification of Protein Foods*, one of those monster volumes with which the shelves of science libraries—and I use the word advisedly—groan. It also is a compilation of the proceedings of an international conference but is rather different from the book I have just described. Not that it does not include a number of chapters of excellent science. For example, S. Kinoshita de-

scribes the developments that have taken place during the past twelve years, mainly in Japan, in the commercial production of amino-acids by fermentation. The manufacture of about 150,000 tons of monosodium glutamate in 1968, more than 80 per cent by fermentation, grew from the identification of an organism, *Corynebacterium glutamicum*, possessing a specific defect in its biochemistry causing it, as Kinoshita calls it, to lose its metabolic balance and accumulate enormous quantities of glutamic acid. It was during the course of this work, which, it should be noted, was done to produce a popular condiment for which there was a good market and not with any particular claim to the salvation of mankind, that it was found that among the auxotrophic mutants of *C. glutamicum* was one capable of accumulating lysine in the fermentation liquor. A good deal is now known of the biochemical mechanism by which this is done and of those by which other organisms can be used to produce threonine, tryptophane, aspartic acid, valine and iso-leucine. Similarly, in another short chapter, E. T. Mertz traces the development of the work, starting from a paper published in 1964, describing the effect of the mutant, Opaque-2, on the amino-acid composition of the proteins in maize endosperm, from which has come the knowledge which enables agronomists today to grow not only maize but barley, rice, wheat, rye and sorghum containing increased lysine and consequently of better nutritional value than before. H. L. Wilcke, too, takes advantage of modern laboratory technique by using a computer to plan mixtures of diverse foods with and without added lysine to provide any predetermined amino-acid pattern at lowest cost.

These sorts of things scientists are qualified to do well, as they are to record the effects on the body weight of weanling male rats of a variety of diets fortified with more or less lysine, threonine, valine or methionine, as D. M. Hegsted so competently describes. But because science is so powerful an implement in the limited area to which it applies, because understanding of the nutritional needs of weanling rats in cages in air-conditioned laboratories allows a crisp biochemical relationship to be drawn within proper statistical limits between the rate of growth and the intake of lysine, it does not follow that the same scientists who plan such experiments, or indeed any scientists at all, are qualified to instruct distant nations of whose history they know little how to achieve the good life. Least of all can the same methods by which in science experiments are aimed towards closely defined targets—maximum live-weight gains of pigs of bacon-weight, let us say—be used to deal with

human affairs. Powdered milk, a remarkable product of high technology, to be sure, is unquestionably a good source of nourishing protein but whether or not the Government of Guatemala best advantaged the nutritional status of its people by spending over two and a half million dollars in buying it, as M. Behar tells us, nutritional scientists—as scientists—are not qualified to judge. And I, for one, feel my blood run cold to read the calculation in the chapter by A. Berg of the Brookings Institute putting forward the argument, and very rationally too, that scientific studies of nutrition, presumably including the fortification of foods with amino-acids, are worthy of support on the basis that “22.5 per cent of the national income of pre-independence India was required to rear children who would not live long enough to make a productive contribution”. Please God the Brookings Institute scientists have not yet got around to making a similar calculation about rearing unproductive post-independence Britons over sixty.

The relative merits of different ways of advancing the nutritional well-being of hard-pressed communities are discussed in considerable detail. Trials with synthetic lysine and techniques for mixing it with cereals or with salt are described; the use of oil-seed residues, of fish protein and of a variety of formulated mixtures. Nor is it overlooked that economics play a part, as well as disease and overcrowding in towns. The difficulties of persuading developing nations to adopt particular population policies are recognized. The primary motivation for large families, writes M. F. Millikan, “is the need to assure that at least one male son will survive”. Throughout the book, however, is the proseletysing faith which is the strong religion of the times which twenty-five years of somewhat qualified progress has done nothing to shake, that science can solve all. D. S. Call can see that the talents of nutritionists and food scientists alone, even when reinforced by economists and statisticians, are insufficient to solve the problems of leading the peoples of the developing countries into the Promised Land. His answer is to call for the enrolment of one more scientist still—an anthropologist.

Nutrition policy is important to the welfare of a nation and nutritionists are important, indeed essential, to its formulation. Yet whether we add chalk to the flour or vitamins to the margarine, whether we provide free milk for the children or not, is not decided in the final analysis by anthropologists or any other scientists. W. H. Sebrell can describe to what extent foods in the United States are fortified with synthetic nutrients but what kind of a medical service the American citizen

shall enjoy is in real life decided by means quite different from the allegedly scientific ones repeatedly advocated in this book. Some of those who attended the conference realized that this was so, to judge from the summary of the debate with which it ended. One very short chapter as well coming late in the book on page 581 draws attention to a point often forgotten by those concerned with what Berg calls “nutrition programming”, that life did go on in history before there were any scientists at all. In it D. B. Jelliffe points out that before the amino-acid fortification of foods was thought of it had in fact been done. In mediaeval Europe people ate mixed wheat and pea flour, in Mexico today they eat corn tortillas and bean frijoles, while Italian peasants sprinkle parmesan cheese on their spaghetti.

Biochemistry of Foods is a modest contribution to the training that turns students into the kind of people that scientists are as illustrated by the two books I have so far discussed. It deals in a straightforward way with some of the biochemical changes that occur when muscle becomes meat and when different kinds of fruit ripen in a store. There is an excellent section on enzymic and non-enzymic browning, another on the technical use of enzymes in the food trades and another again on the microbial deterioration of different foods. Full lists of references are appended to each of these parts. That the scientific rigour of the writing is not particularly strict and that the reader is expected to be familiar with ATP, ADP and the Krebs cycle, yet not know what pectin is, suggests that the book is designed to fit into an already existing syllabus. But if the substantial amount of information it conveys within the scope set by its authors helps to train modest scientists competent in their field, yet aware of its boundaries, it will have served its purpose very well.

MAGNUS PYKE

Plasma Diagnostics

Recent Advances in Plasma Diagnostics. By V. T. Tolok. Vol. 1. Optical Techniques. Pp. vi+130. \$25.20. Vol. 2. Microwave Techniques. Pp. vi+105. \$25.20. Vol. 3. Corpuscular Correlation, Bolometric and Other Techniques. Pp. vi+73. \$15.12. Translated from the Russian by J. R. Büchner. (Consultants Bureau: London and New York, 1971.)

THESE volumes are arranged rather like the proceedings of a conference with short 1,000 to 3,000-word contributions. With this arrangement there is no assessment of the relative merits of the papers nor is there any attempt at an authoritative review of the subject. On the other hand, a wealth of technical detail is included which would not

normally be present in a “review”. The ingenuity and technical adroitness in many of the papers are to be admired and the volumes give a good insight into plasma diagnostics in Russia in the years preceding 1966.

The general standards of translation, typesetting and scientific quality are those appearing, for example, in the *Journal of Experimental and Theoretical Physics*. Not all the technical symbols appear in their standard forms, however. Image intensifiers and converters are referred to as “electron-optic converters” in volume 1, while in volume 2 the term “frequency divider” is more accurately a frequency selective coupler and refers to a device for separating microwave power at different frequencies flowing down a single waveguide. In volume 3, the term “plasma string” could have been more appropriately translated as “plasma column”. There are many references to catalogue numbers of instruments which will be meaningless to the non-Russian researcher.

Judging from the volume on optical techniques, image-intensifiers and converters are in an advanced state of development in the Soviet Union and are widely used. The low density limit to which visible and infrared interferometry has been pushed is in the order 10^{13} to 10^{14} cm⁻³, somewhat lower than is normally associated with these techniques.

This volume somewhat lacks balance on the account that due credit is not given to the dominant role of laser beam scattering techniques both with visible and infrared lasers. Significant omissions, which assuredly would be included in a more recent account, are optical pumping using tunable dye-lasers, the use of Fourier transform techniques in the infrared, and the development of picosecond resolution image intensifiers.

Of the seventeen papers in the volume on microwave techniques, ten are concerned with interferometry of varying degrees of complexity. The remaining seven include one cavity method, one system for studying the behaviour of the surface of a plasma, a paper on theoretical electronics and two papers on lens-aerial design and wall effects. Some of these papers are more in the nature of feasibility demonstrations on the electronics laboratory bench, and only three papers give any detailed account of the results obtained from a plasma device and their interpretation.

The bulk of volume 3, on corpuscular correlation, bolometric, and other techniques, is concerned with analyses of the particle emission from plasma columns, such as charge-exchange neutrals, ions or fusion reaction products. Several of the techniques

described are relevant mainly to the class of plasma devices being studied; while other papers deal entirely with technical aspects and applications of detectors such as surface-barrier semiconductor counters. Perhaps the most interesting contributions are on correlation measurements. From the autocorrelation function of variables such as magnetic field, electric field or light intensity the frequency spectrum of fluctuations and the characteristic size of energy inhomogeneities in a plasma may be derived. This is a powerful technique applicable to plasmas where fluctuations with frequencies in the ultra-high frequency range or lower are quasi-stationary.

The long time-lag between the original work and the present translation means that in these three volumes there is not much that is new for the plasma physicist. He will almost certainly find, however, some rewarding information, mainly technical ideas.

For the newcomer to the subject there exist more appropriate textbooks on plasma diagnostic techniques.

NICOL J. PEACOCK

Piezoelectric Ceramics

Piezoelectric Ceramics. By Bernard Jaffe, William Cook jun., and Hans Jaffe. Pp. ix+317. (Academic: New York and London, October 1971.) £5.50; \$16.

A NUMBER of books and review articles on ferroelectricity and piezoelectricity have appeared during the last few years. In all these books the main emphasis is on the physics of ferroelectricity, as observed in single crystals and on crystal chemical questions. Little is usually said about piezoelectric and ferroelectric ceramics and their applications.

The authors of this excellent book, having worked with piezoelectric and ferroelectric ceramics for many years, are probably the world's experts in this field. It is therefore not surprising that the book is unique. It is well written and covers the whole field competently. The emphasis is on ceramic materials, their properties and their applications. Much information is given on the relation between composition of the ceramics and their electromechanical and ferroelectric properties. Many figures and tables on piezoelectric, elastic and dielectric constants make this book very useful to people who work with these materials. The extensive literature survey makes it a good reference source.

After a chapter on the physics of the piezoeffect in ceramics and a chapter on measurement techniques, the authors devote a long chapter to BaTiO_3 (crystals and especially ceramics) and three chapters to other perovskites and

solid solutions of perovskite ceramics. A chapter on non-perovskite oxides follows. The last two chapters are devoted to questions of manufacturing and applications. They contain a large number of technical details, some of them not published yet.

The book can be recommended without reservation to both scientists and engineers in university and industry. Many questions ranging from fundamental scientific to preparative and applied technological are discussed and answered in this excellent book.

WALTER J. MERZ

Changing Colour

Photochromism: Techniques of Chemistry. Edited by Glenn H. Brown. Vol. 3. Pp. xii+853. (Wiley Interscience: New York and London, November 1971.) £22.25.

PHOTOCHROMISM is an effect associated with compounds which reversibly change their absorption spectra on illumination with light. This is the first comprehensive book on the subject and is a collection of sound review articles on the different categories of photochromism written, with one exception, by industrial scientists.

Livingston writes a brief introductory chapter on photochemical and photophysical phenomena in polyatomic molecules. Some mention of experimental methods (particularly flash photolysis) would have been useful here but will be or are covered by other volumes in the *Techniques of Chemistry* series. Bertelson collects and reviews an impressive amount of information on compounds exhibiting heterolytic cleavage, particularly spiropyrans and triarylmethane dyes. This chapter in particular, and the rest of the book in general, reveals the hidden wealth of data on the subject described in obscure technical reports and patents and which is most usefully mentioned in this book. Other articles on homolytic processes by Eigemann, cis-trans isomerization by Ross and Blanc and tautomerism by Margerum and Miller are lucidly written and the authors have taken considerable care to cover much of the open and hidden literature. Inorganic compounds are discussed in short articles by Deb and Forrestal and by Araujo. Photosynthesis and visual processes feature largely in an excellent description of photochromism in living systems by Vernon and Ke. The final chapter, also by Bertelson, on applications of photochromism shows that much of the basic and applied research in the subject to date has been stimulated by commercial concerns interested in photochromic imaging systems and government agencies requiring a dynamic device for nuclear

flash protection. The book is well edited and should serve as a reference source for some time.

M. A. WEST

Definitions in Science

Dictionary of Science and Technology. Edited by T. C. Collocott. Pp. xvi+1,328. (W. & R. Chambers: Edinburgh and London, 1971.) £6.50.

DICTIONARIES, especially science dictionaries, are all things to all men. To those with a tendency to mis-spell they are simply word lists; for those seeking more information they have to provide definitions that combine an economy of words with considerable lucidity.

That much can be said of all dictionaries. Science dictionaries, on the other hand, have to project not only a meaning but an unambiguous indication of the part of the broad spectrum of science to which that word usually belongs. And entries in a science dictionary must also be adequately cross-referenced, because of the frequent necessity for using other technical words in definitions, or when giving examples. This all adds up to the fact that good science dictionaries are not easy to produce.

The *Chambers Dictionary* categorizes each word into one or more of a hundred subject classifications—some wide ranging (like chemistry) and others surprisingly specific (weaving, for example). In most cases the classification procedure does not lead to ambiguity, but in one case at least the pigeonholing is misleading. The word (particle) accelerator, for example, is classified under "electronics" and defined as a "machine used to accelerate charged particles to very high energies. See also betatron, cyclotron, . . .". Although the entry for betatron gives a classification of nuclear engineering, thus giving the game away, the original definition could easily refer to an exotic valve rather than to an instrument used as a source of particles for nuclear physics experiments. The equivalent definition in *Webster's Third New International Dictionary*, on the other hand, is rather longer, but ends: ". . . charged particles . . . are . . . accelerated . . . until they emerge as a stream of high speed projectiles". Although the *Webster* definition certainly has imperfections, the idea of using the output of an accelerator for nuclear physics has been introduced without making the definition excessively long.

To take a biological example, the *Chambers* definition of hormone is "an internal secretion produced by the endocrine or ductless glands of the body and exercising a specific stimulatory physiological action on other organs to which it is carried by blood. Important hor-

mones are . . .". A similar botanical definition is also given. *Webster* says of "hormone": "a specific organic product of living cells that, transported by body fluids or sap, produces a specific effect on the activity of cells remote from its point of origin". Quite comparably reasonable definitions, by all accounts.

Other reviewers would undoubtedly select other, perhaps more extensive, means of testing for accuracy and lucidity. My guess is that they would all find a few criticisms but that many of these arise because some terms—mathematical ones, for example—are almost impossible to explain in the space of a dictionary definition.

The *Chambers Dictionary of Science and Technology* is by no means outstanding, but it is probably adequate for most of the uses to which it is likely to be put.

R. E. WOODHAM

Ehrenfest in Russia

Paul Ehrenfest. By Victor Jakovlevitch Frenkel (in Russian). Pp. 144. (Atomizdat: Moscow, 1971.) 2.5s; \$0.28.

THE first volume of Ehrenfest's biography, written by M. J. Klein in English, was reviewed in *Nature* in 1970 (*Nature*, **228**, 291; 1970). It seems appropriate to refer here to the independent biography by Frenkel, published a little later, which covers in a considerably smaller space the whole life of this remarkable theoretical physicist until his tragic death in 1933. Those who are masters of the Russian language will read this book with great interest and it would be most profitable for someone to translate it into English.

The reason that this book originated in the USSR is that Ehrenfest, whose scientific development started in Vienna and continued in Göttingen, met at the latter university his wife, Tatiana, a Russian mathematician, and they lived in Petersburg during the years 1907-12. Then, at the age of only 32 years, he became the successor of the great H. A. Lorentz as the sole professor of theoretical physics at Leyden. Obviously his work in Russia impressed those who influenced this selection, and Frenkel emphasizes especially an article on statistical mechanics published by Ehrenfest and his wife in the German *Encyclopedia of Mathematical Sciences* in 1911.

Ehrenfest's fame, however, was based less on his original research accomplishments than on his great ability to look critically at the contemporary problems and to present the results of his analysis both orally in his lectures and in writing in his publications and wide correspondence with the most out-

standing physicists. Chapter 6 in Frenkel's book, entitled "Tell me who your friends are", reports on correspondence and personal encounters especially with Einstein and Bohr, whose differing views Ehrenfest attempted to reconcile.

Not less interesting is the last chapter 8, "The work of the last years", with its emphasis on the history of the discovery of the spin of the electron in 1925 by Ehrenfest's young students Uhlenbeck and Goudsmit, who according to Frenkel owe much encouragement to their teacher.

This chapter ends with the analysis of Ehrenfest's state of deep depression which caused his many travels and, in spite of the warm reception encountered everywhere from his numerous friends, led finally to his voluntary end.

Two appendices (twenty pages of small print) to the attractive main text cover the topics "Statistical Mechanics" and "Ehrenfest's Adiabatic Invariants".

K. FAJANS

Deciding Factors

Decision Theory and Human Behaviour. By Wayne Lee. Pp. x+352. (Wiley: New York and London, October 1971.) £6.15.

To understand human decision-making must be one of the central goals of cognitive psychology. Decisions are ubiquitous components of psychological theories and of everyday experience—whether it is the decision to press a button in a psychological laboratory or on a nuclear missile site, it is clear we stand to gain much from a fuller understanding of the principles and processes that are involved when man makes a decision.

Professor Lee has provided an outstandingly clear account of a wide range of topics in which decision-making plays an important role: studies of subjective probability, utility, gambling, probability learning, signal detection, sequential decision-making and games are all competently reviewed, and what is particularly impressive is the detailed treatment Professor Lee is able to provide without requiring any mathematical sophistication from his readers. Accordingly this book can be strongly recommended for advanced undergraduates and the non-specialist postgraduate.

In spite of the book's clarity, however, or perhaps precisely because of its clarity, it is difficult to avoid a slightly negative overall impression: for all their elegance, most theories that Lee reviews give a rather poor description of human behaviour. One reason for this is that such theories are somewhat isolated from the rest of psychology:

decision theorists are apt to forget, for example, that gamblers have short-term memory difficulties and lapses of attention like the rest of us. Until such information-processing limitations can be fully incorporated within a theory of decision-making, the decision theorist's world will continue to appear artificial.

PHILIP T. SMITH

Studies on Histamine

The Biogenesis and Physiology of Histamine. By Georg Kahlson and Elsa Rosengren. Pp. 318. (Edward Arnold: London, October 1971.) £6.50.

THE strongest point of this book is the emphasis on newer concepts in histamine research, that is, that rates of histamine formation in tissues are of prime importance for evaluating its physiological function(s), that actions of endogenous non-mast cell histamine are neither antagonized by antihistamines nor accurately reproduced by injected histamine, and that new methods, mainly isotopic, are essential to further progress. The text is interesting and well written in Professor Kahlson's highly personal style. The volume was prepared by Kahlson and Dr Elsa Rosengren, an associate at the Institute of Physiology, University of Lund, Sweden, on invitation by the Monograph Committee of the British Physiological Society; it is an account of research on histamine by Kahlson, his colleagues and his students, in the authors' words, "The tale of a journey".

It is stated in the preface that "readers seeking information on a wide realm of histamine physiology will find our account narrow and unsatisfactory". Related work from other laboratories is included, however, so there is adequate coverage of many active research fronts.

The main subject is histamine formation and its relationship to gastric secretion, circulatory control, maintenance of homeostasis, hypersensitivity, pregnancy, wound healing, malignant and regenerative growth, protein synthesis and seed germination. Methods for determination of histamine formation and effects of inhibitors and of hormones are included, as are chapters on histamine catabolism, brain histamine and a short discussion of mast cells.

Aspects of research on histamine omitted, or given only minor emphasis, are its chemistry, isolation from natural sources, methods not used by Kahlson's group, pharmacological actions, release, toxicity, tolerance and binding to proteins.

Kahlson and Rosengren cite 476 references, some as late as 1970. The book is the only recent one in its field and is highly recommended for those interested in histamine research.

RICHARD W. SCHAYER

CORRESPONDENCE

Limits of Growth

SIR,—As a member of the Club of Rome, I have been able to read a pre-publication copy of Dr Dennis L. Meadows's study *The Limits to Growth* which you castigated in an editorial (*Nature*, **236**, 47; 1972) a month or more before it will become available to most of your readers. May I assure them that there is a good deal more to be said for it than your thunderings implied?

In the first place, Dr Meadows emphasizes several times that these studies should not be interpreted as predictions. What he is trying to do is to examine and illustrate the modes of behaviour of a complex system involving both positive and negative feed-backs when it is subjected to sudden alterations in inputs. Broadly speaking, he is investigating the transients which may occur on the way towards a new equilibrated pathway (or chreod, in my terminology). And when such transients could take the form of doublings or halvings of the world population in periods of a few decades, they are of more human concern than the word "transients" may at first suggest.

There are, of course, many real and important questions to be asked about this preliminary study. How robust are the demonstrated modes of behaviour against variations in the coefficients assigned to measure the strength of the various interactions involved? One would have wished Meadows to have provided more definite evidence on this point, but personally, having spent much of my life studying the highly "canalized" processes of biological development, I find fairly plausible his assurance that such variations (within reasonable limits) rarely alter the modes of behaviour and usually only produce minor alterations in the timing of them.

Probably a more serious question is

one alluded to, in somewhat superior tones, by the editor of *Nature*, namely that this is a very "aggregated" study. It lumps together, not only nations and regions of very different characters into global totals of population, food production and so on, but also aggregates together various sorts of production, for example, housing and the infrastructures of urbanization with more ephemeral and less necessary consumer goods. Further distinctions within some of the broad categories employed by Meadows will certainly be very necessary. Indeed, I think he would be first to admit so; and further work, sponsored by the Club of Rome, is already attempting refinements of this sort. The results of these developments will be awaited with interest by all those, who I think will be many, who feel that Dr Meadows has taken an interesting first step in one of the few directions which seem to offer hope of a rational understanding of the complex world system.

Yours faithfully,

C. H. WADDINGTON

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Breast Cancer

SIR,—With great interest we read the editorial on the possible viral aetiology of human breast cancer (*Nature*, **235**, 7; 1972). You mentioned a statement in which Spiegelman would advise women from breast cancer families not to nurse in case they had virus in their milk. As an objection to this thought you pointed out other possible routes of vertical transmission, referring to the work of the "Dutch school of RNA tumour virologists" on the murine counterpart of the human breast cancer virus.

In our studies we emphasized the role

of the gametes in the transmission of various murine mammary tumour virus strains. However, we observed that if mice are prenatally infected with such a virus, additional milk borne infection has an accelerating effect on mammary tumour development. In addition, female mice which are heterozygous for spontaneous release of a gamete borne virus can infect their offspring either genetically or with their milk; that is, if a daughter does not carry the gene for virus release, she still may develop a mammary tumour because she was infected the other way.

These two observations may support those who want to abolish breast feeding by virus-carrying mothers. But one must also take into consideration that we only found transfer of the virus if large numbers of virus particles are present in the milk. As far as we know in most human milks the amount of virus is low. Often a hundred times more would be necessary to have effect in the murine situation. In our opinion the advice of Spiegelman could be moderated in that it might be given to those women who have a great deal of virus in their milk.

However, a further problem is that prolonged lactation has a protective effect on the mammary gland with regard to carcinogenesis. By not nursing, a mother may either save her child from getting breast cancer or at least delay it, but at the same time she promotes the chance that she will get the disease herself. Therefore, discussion of breast feeding seems rather academic, particularly in view of the many other aspects of breast feeding which are not related to the cancer problem.

Yours faithfully,

P. BENTVELZEN

*Radiobiological Institute TNO,
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Obituary

Professor G. Ya. Bei-Bienko

THE prominent Soviet biologist, Professor G. Ya. Bei-Bienko, died on November 2, 1971, after a short illness. He was President of the Entomological Society of the USSR Corresponding Member of the Academy of Sciences of the USSR and holder of several state awards. He was also President of the

last International Congress of Entomology, held in Moscow in 1968.

Professor Bei-Bienko was born on February 7, 1903, in the small Ukrainian town of Belopolie. His family, who were shoemakers, moved soon afterwards to Omsk in Siberia, and it was here that he went to school and later to the Omsk Agricultural Institute. After graduating he joined the staff of the Institute and later

became Lecturer in Applied Entomology there.

During his childhood Bei-Bienko accompanied his father on many of his business trips in Siberia and it was during these travels that he developed the love for nature—and particularly the interest in insects—that was to last for the rest of his life. While still a student he became interested in the orthoptera and, after making a list of

the acridoidea of the Omsk region, he went on to study their ecology. In later years he divided his interest between the taxonomy and ecology of orthopteroid insects.

In 1927 Bei-Bienko moved to Leningrad, where he was to spend the rest of his life, and began work in the Zoological Museum of the Academy of Sciences of the USSR. Although always retaining a close connexion with this museum, he moved in 1929 to the Plant Protection Institute of the USSR and in 1938 to the Leningrad Agricultural Institute, where he held the chair of general entomology until his illness last year. While working in Leningrad Bei-Bienko published several major works on the systematics of the dictyoptera, dermaptera, tettigonioida and acridoidea of the USSR, and at the same time produced many papers on the applied entomology and ecology of these groups. He took part in many expeditions, both within the USSR and to other Asiatic countries, and this resulted in the publication of a number of faunistic studies.

During the siege of Leningrad in the Second World War, Bei-Bienko took an active part in defending the city, and it was only when he became completely exhausted that he was evacuated to Perm, where he remained until the end of the war.

Professor Bei-Bienko will be remembered not only for his substantial contributions to science, but also for the warmth and good humour of his personality. He was a man of remarkable energy and remained fully active in his scientific work until the year of his death.

Mr Michael Graham



MICHAEL GRAHAM, a former Director of Fishery Research in the Ministry of Agriculture, Fisheries and Food, died on January 1, aged 73.

He will be remembered firstly as a distinguished marine scientist who was largely responsible for the development

of British fishery research after the Second World War to a position of world renown, and secondly, as a man who appreciated the importance of ecological studies and the need for conservation of natural resources many years before such ideas attained their present importance and, what is more, took practical steps to translate his ideas into action. But to those who worked with him he will also be remembered as a man of deep sympathy and understanding. This is clear from his books and it dominated his personal relations. Never could there have been a better mentor to lead the young biologist through the intricacies of fisheries research and its applications.

After service in the Royal Navy during the First World War Michael Graham went to Cambridge to read Natural History and joined the staff of the Fisheries Laboratory, Lowestoft, in 1920. At first he worked mainly on the biology of the North Sea cod, and in particular studied its life history and fluctuations in the size of the stock.

Between 1927 and 1928 these studies were interrupted by a period of work in East Africa to carry out fishing survey of Victoria Nyanza. This was concerned with the study of the distribution of the important food fish, *Tilapia esculenta*, and the danger of its being over-fished, and it resulted in the formulation of a series of recommendations to the appropriate governments. This was a period of fruitful collaboration with E. B. Worthington and the expedition started a movement whereby fishery science, which had been developed in the seas, became applied to large lakes, especially those in the tropics. The study of Victoria Nyanza stimulated other surveys and from them has emerged, over the years, a large and flourishing fishing industry as well as much research which has revealed some of the fundamental processes of biological production.

In both his North Sea and Victoria Nyanza studies Graham had been concerned with the problem of rational fishing, and in the 1930s he became concerned with the general problem of the dynamics of exploited fish populations. In this he followed the lead given by his director, E. S. Russell. He assumed that the growth of a fish population took the form of the logistic curve observed for other populations and from this concluded that the most effective level of fishing is that which maintains the population at an abundance equal to about one half that of the virgin stock. Outside the laboratory he found time during this period to study, experiment in and write about soil and grassland management.

After service in the RAF during the Second World War Michael Graham was appointed Director of Fishery

Research and was responsible for the Ministry's fishery research programme until he retired in 1958. This period was particularly noteworthy for the impetus which he gave to the mathematical studies of fish populations by recruiting to the Lowestoft laboratory and encouraging the work of men like Beverton, Holt and Gulland. He also played a prominent part in obtaining intergovernmental agreement concerning fish conservation in the North Sea and elsewhere. Other milestones during his directorship were the establishment of the Ministry's fisheries radiobiological laboratory at Lowestoft and its shellfish research laboratory at Burnham-on-Crouch, and the development of a comprehensive research programme in distant waters, especially the Barents Sea, based on cruises carried out in all seasons of the year by the research vessel Ernest Holt.

After retirement he carried out highly successful pioneer work on the reclamation of slag heaps in Lancashire and his experiments showed that they could be "greened over" at very little cost. He also became a special lecturer in biology at Salford University from 1966 to 1971 and delighted in expressing in lecture and book form the importance of ecology and in illustrating his theme with practical examples culled from various parts of his own career.

Announcements

University News

Professor E. J. H. Corner, University of Cambridge, has been appointed Royal Society Leverhulme visiting professor to the **National Biological Institute**, Bogor, Indonesia, for a period of 7 months.

Dr V. Dubowitz, University of Sheffield, has been appointed to the chair of paediatrics at the Institute of Child Health, attached to the Royal Postgraduate Medical School, **University of London**.

Dr C. J. Stairmand has been appointed to an industrial chair in the Department of Chemical Engineering, **Loughborough University of Technology**.

Appointments

Professor R. E. O. Williams has been appointed director of the **Public Health Laboratory Service** in succession to **Sir James Howie**, who will retire in September 1973.

Miscellaneous

The **Institution of Mechanical Engineers** will award annually a senior James Clayton fellowship, for project or study programmes in specific areas of mechanical

engineering. The suggested topics for 1972 are a review of the problems of recycling industrial waste and the supply of water for industrial and domestic use, or a review and assessment of the available and developing techniques for communicating engineering information. The award is worth £3,000 annually, plus expenses, and will normally be made for a period of two years or less. Further information and forms of application can be obtained from the Education Officer, Institution of Mechanical Engineers, 1 Birdcage Walk, Westminster, London SW1H 9JJ.

The following awards have been made by the **Royal Geographical Society** for 1972: Founder's medal, to Rear-Admiral G. S. Ritchie, formerly hydrographer of the Navy, for hydrographical charting and oceanographical exploration; Patron's medal, to Dr M. D. Gwynne, University of Oxford, leader of the Society's South Turkana (NW Kenya) Expedition 1967–70; honorary membership to M. Jean Monnet, for distinguished services to the economic planning and development of Europe; Victoria medal, to Professor G. H. J. Daysh, formerly of the University of Newcastle upon Tyne; Cherry Kearton medal and award, to David Attenborough, director of programmes, BBC Television; Murchison award, to Professor W. G. East, University of London; Back award, to Dr D. R. Harris, University of London; Cuthbert Peek award, to Dr Anthony Young, University of East Anglia; Gill memorial, to Professor D. Harvey, Johns Hopkins University; Ness award, to Major D. N. Hall, leader of the British Expedition to the Afr Mountains 1970.

Corrigendum

IN the article entitled "Oxygen Isotope Profiles through the Antarctic and Greenland Ice Sheet" by S. J. Johnsen, W. Dansgaard, H. B. Clausen and C. C. Langway, jun. (*Nature*, **235**, 429; 1972), an important paragraph was accidentally omitted. This read: "The concept of the (West) Antarctic ice sheet being exposed to considerable changes in thickness is further supported by the fact that the δ s in the lower part of the Byrd core should be much lower than observed, if the deep ice were originally deposited at altitudes between 2,000 and 2,500 m, that is, some 500 to 1,000 m higher than the present surface altitude at Byrd (Fig. 4a). If we assume that the climatic conditions 81,000 years ago were essentially like those of today, and if we tentatively use the present isotopic altitude effect in the inner of Antarctic (-1‰ per 100 m increasing altitude)¹, the lowest part of the δ curve in Fig. 5c and 5d should be 10‰ lower. This difference suggests that the West Antarctic ice sheet was nearly 1,000 m lower than shown in Fig. 4, which would explain the

Barbados I high sea level² (Fig. 5e). The reason for the proceeding decrease of the Byrd δ record would then seem to be a slow build-up to greater thickness combined with (and caused by) cooling climate. The North Greenland ice sheet is probably much more stable, because the temperature of most of the subsurface is below the melting point, and because warm (cold) climate is associated with more (less) maritime conditions with higher (lower) accumulation. This latter effect has been accounted for in the correction of the Camp Century time scale."

¹ Gonfiantini, R., Togliatti, E., de Breuck, W., and Picciotto, E., *Nature*, **197**, 1096 (1963).

² Broecker, W. S., Thurber, D. L., Goddard, J., Ku, T. L., Matthews, R. K., and Mesolella, K. J., *Science*, **159**, 297 (1968).

International Meetings

April 13–14, **Biochemical Society Meeting**, Cardiff (The Biochemical Society, 7 Warwick Court, Holborn, London WC1R 5DP).

April 17, **Unorthodox Views of the Initiation of Cationic Polymerization**, Keele (Dr P. H. Plesch, Department of Chemistry, University of Keele, Keele, Staffordshire).

April 18, **Joint Meeting of the Collagen and Mucopolysaccharide Clubs**, Birmingham (Dr A. J. Bailey, ARC Meat Research Institute, Langford, Bristol).

April 18–21, **Transportation Engineering**, London (Conference Officer, Transportation Conference, Institution of Civil Engineers, Great George Street, Westminster, London SW1P 3AA).

April 21–22, **Protein Metabolism and Hormones**, Southampton (The Nutrition Society, Chandos House, 2 Queen Anne Street, London W1).

April 24–25, **Combustion Problems in Industry and Agriculture**, Seattle, Washington (Dr R. P. Wilson, Dynamic Science, 2400 Michelson Drive, Irvine, California 92664, USA).

April 24–26, **Particle Growth in Suspensions**, London (Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London SW1).

April 24–27, **Chemical Vapour Deposition**, Salt Lake City (Fred A. Glaski, Programme Chairman, Fansteel Inc., 10258 Norris Avenue, Pacoima, California 91331, USA).

April 24–29, **Experimental Behaviour Basis of Mental Disturbance**, Galway (Dr W. J. E. Jessop, Medical Research Council of Ireland, 9 Clyde Road, Dublin 4, Ireland).

April 25–27, **Scanning Electron Microscopes**, and workshop on **Biological Specimen Preparation for Scanning Elec-**

tron Microscopy, Chicago (Dr Om Johari, IIT Research Institute, 10 West 35th Street, Chicago, Illinois 60616, USA).

April 25–28, **Computer Aided Design**, Southampton (Manager, IEE Conference Department, Savoy Place, London WC2R 0BL).

April 26, **Local Interests in Powder Characterization**, Bristol (Society for Analytical Chemistry, 9–10 Savile Row, London W1X 1AF).

April 30–May 6, **Stereochemistry**, Bürgenstock, near Lucerne (Professor W. D. Ollis, Department of Chemistry, The University, Sheffield S3 7HF).

April 30–May 20, **Waste Recovery by Microorganisms**, Kuala Lumpur (Professor W. R. Stanton, University of Malaya, Pantai Valley, Kuala Lumpur, Malaysia).

May 9–11, **Uses of Aluminium in Electrical Engineering**, Renfrew (Manager, Conference Department, IEE, Savoy Place, London WC2R 0BL).

May 9–19, **Mechanical Handling Exhibition**, London (ITF-Iliffe Exhibitions Limited, Commonwealth House, New Oxford Street, London WC1A 1PB).

May 10, **Traffic Engineering and Planning**, Huddersfield (Secretary and Registrar, Institute of Mathematics and its Applications, Maitland House, Warrior Square, Southend on Sea, Essex SS1 2JY).

May 11, **Europe—British Food Technology on the Threshold**, London (Mrs L. Dawes, Assistant Secretary, Institute of Food Science and Technology, 41 Queen's Gate, London SW7).

May 11–13, **X and Gamma-ray Astronomy** (non-solar), Madrid (COSPAR, Apartado de Correos 8454, Madrid 8, Spain).

May 14–17, **Medical Technology Exhibition**, Stuttgart (CES Overseas Limited, Bridge House, 181 Queen Victoria Street, London EC4).

May 15–19, **Neutron Dosimetry in Biology and Medicine**, Munich (Symposium Sekretariat, Gesellschaft für Strahlen und Umweltforschung mbH, D-8042 Neuherberg, b. München, Ingolstadter Landstrasse 1, Germany).

May 17–19, **Gas Chromatography—Mass Spectrometry**, Isle of Elba (Dr Alberto Frigerio, Istituto di Ricerche Farmacologiche "Mario Negri", Via Eritrea 62, 20157 Milan, Italy).

May 19, **Fluorescence Microscopy in Chromosome Studies, Virology and Immunology**, Birmingham (Professor D. G. Harnden, Department of Cancer Studies, University of Birmingham, Birmingham B15 2TJ).

May 19–21, **Cost Reduction in Information Systems**, Dayton (Frank Slater, Technical Program Chairman, G-27 Hillman Library, University of Pittsburgh, Pittsburgh, Pennsylvania 15213, USA).

Reports and Publications

not included in the Monthly Books Supplement

Great Britain and Ireland

- University of Oxford. Nuffield Committee for the Advancement of Medicine—Annual Report 1970. (Supplement No. 1 to the *University Gazette*, Vol. cii, January 1972.) Pp. 20. (Oxford: The University, 1972.) 40p. [241]
- Journal of Human Evolution*, Vol. 1, No. 1, January 1972. Pp. 1–136. Published six times yearly. Subscription: UK £12.50 plus 75p postage; Overseas £14.60 plus 75p postage. (London and New York: Academic Press, 1972.) [241]
- The Forensic Science Society. World List of Forensic Science Laboratories. Second edition. Pp. 96. (London: The Forensic Science Society, 1972.) £1.50; \$4. [251]
- The Industrial Council for Educational and Training Technology. Annual Report 1970–1971. Pp. 16. (London: ICETT, 1972.) [251]
- Environmental Care: The Raising of Environmental Standards. Pp. 92. (Liverpool: City of Liverpool Environmental Health and Protection Department, 1972.) [251]
- Royal Observatory Bulletins, No. 169: Motion of A0 Stars Perpendicular to the Galactic Plane. V. (U,B,V) Photometry of A Stars in the South Galactic Cap. By J. B. Alexander and B. S. Carter. Pp. 353–362. (Hertmonceux: Royal Greenwich Observatory, 1971.) 20p net. [251]
- Working for Nature—Council for Nature Report 1970/1971. Pp. 17. (London: Council for Nature, 1972.) [261]
- Department of Education and Science. Science Policy Studies, No. 5: An Analysis of Equipment Costs in University Science and Engineering Departments. Pp. viii+38. (London: HMSO, 1972.) 32p net. [261]
- British Antarctic Society. Scientific Reports No. 70: Geomorphology of the Stromness Bay—Cumberland Bay Area, South Georgia. By Chalmers M. Clapperton. Pp. 25+5 plates. (London: British Antarctic Survey, 1971.) £1.75 net. [271]
- Natural Gas on Target: Borrowing Powers for the Proposed British Gas Corporation. Pp. 16. (London: The Gas Council, 1971.) [271]
- Natural Environment Research Council. Institute of Geological Sciences. Assessment of British Sand and Gravel Resources No. 1: The Sand and Gravel Resources of the Country South-East of Norwich, Norfolk. (Description of 1:25,000 Resource Sheet TG20. Report No. 71/20.) By E. F. P. Nickless. Pp. vi+94. (London: HMSO, 1971.) £1.15 net. [271]
- Natural Environment Research Council. Institute of Geological Sciences. British Regional Geology—The South of Scotland. Third edition. By D. C. Greig. Pp. 125+13 plates. (Edinburgh and London: HMSO, 1971.) 50p net. [281]
- National Science Council; Royal Irish Academy. Register of Scientific Research Personnel. Compiled by D. Murphy and D. O. Brochain. Pp. xiii+176. (Dublin: Government Publications Sales Office, GPO Arcade, 1972.) 32p. [281]
- Amino-acid, Peptide and Protein Abstracts*, Vol. 1, No. 1, January 1972. Pp. 1–100. Annual subscription including indexes: Europe £40; Outside Europe by airmail US \$150. (London: Information Retrieval Limited, 1972.) [281]
- Britain's Natural Gas. Pp. 48. (London: The Gas Council, 1972.) [311]
- London School of Hygiene and Tropical Medicine. Report on the work of the School, 1970/1971. Pp. 111. (London: London School of Hygiene and Tropical Medicine, 1972.) [311]

- Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 271, No. 1213 (27 January, 1972): A Discussion on Volcanism and the Structure of the Earth. Organized by J. Sutton, P. A. Sabine and R. R. Skelhorn. Pp. 101–323. (London: The Royal Society, 1972.) £5.90; \$15.40. [311]
- The Complete Statistician. By Professor Frank Downton. (An Inaugural Lecture delivered in the University of Birmingham on 2 March 1971.) Pp. 19–20p. Good History and Bad. By Professor R. H. C. Davis. (An Inaugural Lecture delivered in the University of Birmingham on 11 November 1971.) Pp. 13; 25p. (Birmingham: The University, 1971 and 1972.) [311]
- Admiralty Marine Science. Publication No. 13: Oceanographic Observations in the Indian Ocean West of Fumatra. *C.S. Cable Enterprise*, February–March 1967. Pp. 17+48 figures. (Taunton: Hydrographic Department, Ministry of Defence, 1971.) [311]
- Unemployment: The Grim Truth and the Way Out. Food for Thought: Can Britain Survive without Redeployment of Labour? By Noel Armstrong. Pp. 8. (Norwich: Noel Armstrong, 3 Eaton Road, 1972.) 3p. [311]
- The Training of Teachers of Science and Mathematics. Pp. 55. (London: The Royal Society, 1972.) [311]
- Philosophical Transactions of the Royal Society of London. A: Mathematical and Physical Sciences. Vol. 271, No. 1214 (27 January 1972): The Swirling Vortex. By J. Serrin. Pp. 325–360+plates 2–4. £1.20; \$3.10. Vol. 271, No. 1215 (27 January 1972): Lunar Crater Origin in the Maria from Analysis of Orbiter Photographs. By G. Fielder, R. J. Fryer, C. Titulaer, A. K. Herring and B. Wise. Pp. 361–409+plates 5–7. £1.50; \$3.90. (London: The Royal Society, 1972.) [311]
- Reconciling Physics with Reality. By Professor A. B. Pippard. (Inaugural Lecture delivered at a meeting of the Cambridge University Physics Society on 7 October 1971.) Pp. 40. (London: Cambridge University Press, 1972.) 40p; \$1.45. [12]

Other Countries

- Fisheries Research Board of Canada. Technical Report No. 287: The Influence of Synthetic Surfactants on the Functional Properties of the Olfactory Epithelium of Atlantic Salmon. By A. Sutterlin, N. Sutterlin and S. Rand. Pp. 7. (St. Andrews, New Brunswick: Fisheries Research Board of Canada, Biological Station, 1971.) [181]
- Commonwealth of Australia. Department of Supply. Australian Defence Scientific Service. Defence Standards Laboratories Technical Note No. 206: An Investigation into the Discoloration of Victorian Hardwood Panels. By L. A. Hill, R. Hancox and N. McKenzie. Pp. 18. (Ascot Vale, Victoria: Defence Standards Laboratories, 1971.) [191]
- Unesco. Educational Studies and Documents, No. 5: Literacy for Working—Functional Literacy in Rural Tanzania. By Margo Viscusi. Pp. 39. (Paris: Unesco, 1971.) 4 francs; 30p; \$1. [211]
- Organization for Economic Cooperation and Development. Reviews of National Science Policy—Switzerland. Pp. 253. (Paris: OECD; London: HMSO, 1971.) 28 francs; £2.15; \$6.25. [211]
- Smithsonian Contributions to Zoology, No. 90: Criteria for Analysis and Interpretation of the American Fish Genera *Nocomis* Girard and *Hybopsis* Agassiz. By Robert E. Jenkins and Ernest A. Lachner. Pp. 15. 30 cents. No. 92: Populations of the Polyploid Species *Nocomis leptoccephalus* (Girard) with a Description of a New Subspecies. By Ernest A. Lachner and Martin L. Wiley. Pp. 35. 45 cents. (Washington, DC: Smithsonian Institution Press, 1971. For sale by US Government Printing Office.) [211]

- Canada: Department of Energy, Mines and Resources. Geological Survey of Canada. Paper 70-14: Middle Devonian Tectonic History of the Tathlina Uplift, South District of Mackenzie and Northern Alberta, Canada. By H. R. Belyea. Pp. iv+38. Paper 70-54: Uranium in Stream Sediments in Carboniferous Rocks of Nova Scotia. By H. W. Little and C. C. Durham. Pp. v+17. \$1.50. Paper 71-25: Dendrochronological Techniques Used by the Geological Survey of Canada. By M. L. Parker. Pp. iv+30. \$1.50. (Ottawa: Information Canada, 1971.) [211]
- US Department of the Interior: Geological Survey. Bulletin 1354-A: Changes in Stratigraphic Nomenclature by the US Geological Survey, 1970. By George V. Cohee, Robert G. Bates and W. B. Wright. Pp. iii+38. 30 cents. Water-Supply Paper 1798-H: Sediment Transport by Streams in the Chehalis River Basin, Washington, October 1961 to September 1965. By P. A. Glancy. Pp. iv+53. Professional Paper 636: Geology of the Coamo Area, Puerto Rico, and Its Relation to the Volcanic Arc-Trench Association. By Lynn Glover, III. Pp. iv+102+4 plates. (Washington, DC: Government Printing Office, 1971.) [211]
- Anuario del Observatorio Astronómico de Madrid para 1972. Pp. 384. (Madrid: Observatorio Astronómico, 1972.) [241]
- Académie Royale de Belgique. Classe des Sciences. Mémoires, Tome 39, Fasc. 6: Régénération d'un Ascidiote de *Clavelina lepadiformis* Müller par un Fragment de Stolon et par un Thorax Isolé. Par Paul Brien. Pp. 92. (Bruxelles: Académie Royale de Belgique, 1971.) 260 francs. [261]
- Commission on Post-Secondary Education in Ontario. Draft Report. Pp. 112. (Toronto: Commission on Post-Secondary Education in Ontario, 1971. Available free from the Queen's Printer Bookstore, 880 Bay Street, Toronto.) [271]
- US Department of the Interior: Geological Survey. Bulletin 1324-D: The Chopawamsic Formation—a New Stratigraphic Unit in the Piedmont of Northeastern Virginia. By D. L. Southwick, John C. Reed, Jr., and R. B. Mixon. Pp. iii+11. 10 cents. Professional Paper 393-C: Foraminifera from the Pierre Shale (Upper Cretaceous) at Red Bird, Wyoming. Pp. iii+54+7 plates. \$1. Professional Paper 646-A: Complete Bouguer Gravity and General Geology of the Cape San Martin, Bryson, Piedras Blancas, and Sam Simeon Quadrangles, California. By Stephen H. Burch. Pp. iii+12+1 plate. Professional Paper 863-C: Foraminifera from the Bahama Bank West of Andros Island. Pp. iii+22+3 plates. 50 cents. (Washington, DC: Government Printing Office, 1971.) [281]
- University of California, San Diego. Scripps Institution of Oceanography—Annual Report for the two years ending June 30, 1970. Pp. 62. (La Jolla, California: Scripps Institution of Oceanography, 1971.) [281]
- University of Queensland Papers, Vol. 1, No. 4: Shallow Water Demospongiae from Heron Island. By Patricia R. Bergquist. (Great Barrier Reef Committee, Heron Island Research Station.) Pp. 63–72. 40 cents. (St. Lucia, Qd.: University of Queensland Press, 1969.) [311]
- Smithsonian Contributions to Palaeobiology, No. 9: Catalog of Type Specimens of Invertebrate Fossils: Conodonts. Compiled by Frederick J. Collier. Pp. 256. \$2.50. Smithsonian Contributions to Zoology, No. 58: Keys to the Hawaiian Marine Gammaridea, 0–30 Metres. By J. Laurens Barnard. Pp. 135. \$1.75. (Washington, DC: Smithsonian Institution Press, 1971. For sale by US Government Printing Office, 1971.) [311]
- Mitteilungen aus der Biologischen Bundesanstalt für Land- und Forstwirtschaft, Berlin-Dahlem. Heft 142: Methoden zur Konzentrations-messung von Methylobromid im Vorratsschutz. Von Dr. Richard Wohlgenuth. Pp. 33. (Berlin-Dahlem: Biologische Bundesanstalt für Land- und Forstwirtschaft, 1971.) [311]

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